```
=> d his
     (FILE 'HOME' ENTERED AT 16:23:16 ON 16 AUG 2001)
    FILE 'HCAPLUS' ENTERED AT 16:23:25 ON 16 AUG 2001
            25 S FRIEDE M?/AU
L1
            19 S HERMAND P?/AU
L2
            39 S L1-2
L3
            16 S L3 AND ADJUVANT
L4
             3 S L4 AND POLYOXY?
                                                           INVENTOR SEARCH
              SELECT RN L5 1-3
    FILE 'REGISTRY' ENTERED AT 16:25:09 ON 16 AUG 2001
L6
            29 S E1-29
    FILE 'HCAPLUS' ENTERED AT 16:25:20 ON 16 AUG 2001
            3 S L5 AND L6 3 cites w/ 29 compounds displayed
L7
    FILE 'REGISTRY' ENTERED AT 16:28:42 ON 16 AUG 2001
            14 S L6 AND PMS/CI 14 cpds from inventor that are polyoxy polymers
15 S L6 NOT L8
L9
L10
             1 S L9 AND "TETRA"
L11
L12
             4 S L10-11
L13
            11 S L9 NOT L12
L14
             1 S L13 AND "OCTA"
             5 $ L12 OR L14 = 5 cpds fr. inventor that are poly oxy cpds
L15
        207440 S PETH/PCT
L16
L17
        154158 S PES/PCT
    FILE 'HCAPLUS' ENTERED AT 16:33:12 ON 16 AUG 2001
        108766 S L8 > Searching applicants cpds
L18
L19
          9892 S L18(L)THU/RL
L20
L21
         26016 S ADJUVANT
         48314 S VACCIN?
L22
            73 S L20(L)L21
L23
        416391 S AQUEOUS (3A) SOLUTION
L24
L25
         51337 S MICEL?
L26
             5 S L23 AND L24-25
L27
             5 S L26 NOT L7
         28271 S LT OR CT OR 3D-MPL OR CPG OR QS21
L28
L29
             1 S L28 AND L27
                             1 cit
L30
             4 S L27 NOT L29
L31
             5 S L23 AND L28
L32
             4 S L31 NOT L27
L33
             3 S L32 NOT L7
L34
           250 S L18(L)L21
L35
            16 S L34 AND L24-25
            13 S L35 NOT EMULS?
L36
L37
            10 S L37 NOT (L7 OR L36 OR L27 OR L28)
L38
        388311 S ?ACRYLAT? OR ?ACRYLIC
L39
            10 S L38 NOT L39
L40
         81791 S VESIC?
L41
         36342 S POLYOXYETHYLEN?
L42
L43
L44
           144 S L43(L)L21-22
L45
            13 S L44 AND L24-25
L46
            2 S L28 AND L44
L47
             0 S L45 AND L46
            13 S L45-46 NOT (L7 OR L36 OR L27 OR L28 OR L42) 13 cite 5
```

T : Subject: STIC-ILL

REF. ORDER FOR 09/647,518

PLEASE PROVIDE ME WITH A COPY OF EACH OF THE FOLLOWING REFERENCES. THANKS.

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J. COLLOID INTERFACE SCI. (1998) 197(1), 48-56.

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M. CEPERLEY

AU 1641

MAIL BOX: CM1-7E12

OFFICE: CM1-8D15

308-4239

09/647,518

```
=> d bib abs hitstr 1
     ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS
1.7
     2001:228739 HCAPLUS
ΑN
     134:271227
ТΤ
     Vaccines containing polyoxyethylene sorbitan ester surfactant
     adjuvants
IN
     Friede, Martin; Hermand, Philippe; Henerickx,
     Veronique
     Smithkline Beecham Biologicals S.A., Belg.
PA
SO
     PCT Int. Appl., 25 pp.
     CODEN: PIXXD2
DΤ
     Patent
     English
FAN.CNT 3
     PATENT NO.
                        KIND DATE
                                               APPLICATION NO. DATE
                               -----
     -------
                        ----
                                                ------
     WO 2001021207
                               20010329
PΙ
                         A2
                                               WO 2000-EP9366
                                                                  20000922
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CR, CU, C2, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
              HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
              SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
              YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
22703 A 19990924
PRAI GB 1999-22703
     GB 2000-16685 A 20000706
The invention relates to a novel adjuvant system comprising a
     polyoxyethylene sorbitan ester surfactant in combination with
     octoxynol and vaccines comprising the adjuvant system together
     with an antigen. Further provided are methods of manufg. the
     adjuvants and vaccines and the use of the adjuvants and
     vaccines in the prophylaxis or therapy of disease. Examples were given
     for methods used to measure antibody responses in sera and effect of Tween 80 and Triton on the intranasal immunogenicity of inactivated whole
     influenza virus in mice.
ΙT
     207751-21-1
     RL: PRP (Properties)
         (unclaimed nucleotide sequence; vaccines contg. polyoxyethylene
         sorbitan ester surfactant adjuvants)
RN
     207751-21-1 HCAPLUS
     DNA, d(T-C-G-T-C-G-T-T-T-G-T-C-G-T-T-T-T-G-T-C-G-T-T) (9CI) (CA INDEX
CN
     NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     81-25-4D, Cholic acid, derivs. 9002-93-1, Triton X-100
     9005-63-4D, Polyoxyethylene sorbitan, esters 9005-65-6, Tween 80
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
         (vaccines contg. polyoxyethylene sorbitan ester surfactant
         adjuvants)
     81-25-4 HCAPLUS
RN
     Cholan-24-oic acid, 3,7,12-trihydroxy-, (3.alpha.,5.beta.,7.alpha.,12.alph
CN
     a.)- (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

RN 9002-93-1 HCAPLUS

Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME) CN

$$\begin{array}{c|c} \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me} & \text{Me} \end{array}$$

RN 9005-63-4 HCAPLUS

Sorbitan, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME) CN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN

9005-65-6 HCAPLUS Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs. CN(9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

J. . * '

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=> d bib abs hitstr 2
L7
     ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS
     2001:228686 HCAPLUS
AN
DN
     134:271249
TΤ
     Adjuvant comprising a polyoxyethylene alkyl ether or
     ester and at least one nonionic surfactant
     Friede, Martin; Hermand, Philippe; Henderickx,
     veronique
PΑ
     Smithkline Beecham Biologicals S.A., Belg.
SO
     PCT Int. Appl., 35 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 3
     PATENT NO.
                        KIND DATE
                                               APPLICATION NO. DATE
PI
     WO 2001021152
                         A1
                               20010329
                                               WO 2000-EP9368
                                                                  20000922
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
              HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
              LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
              SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
              CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI GB 1999-22700
                               19990924
                         Α
                               20000706
     GB 2000-16647
                         Α
OS
     MARPAT 134:271249
     The present invention relates to a novel adjuvant system
AB
     comprising a polyoxyethylene alkyl ether or ester surfactant in
     combination with at least 1 addnl. nonionic surfactant. Preferably, the addnl. nonionic surfactant is an Octoxymel (the Triton series). The present invention provides the novel adjuvants, vaccines
     comprising them, and methods of their manuf. and their formulation into
     vaccines. The use of the adjuvants or vaccines of the present
     invention in the prophylaxis or therapy of disease is also provided. The effect of adding Triton X100 to a low and sub-optimal dose of Laureth-9 on
     the intranasal boosting of tetanus toxoid (TT)-specific serum antibodies
     was evaluated. Female balb/c mice were primed i.m. with 20% (2x50 pl) of
     the human dose of the com. DTPa vaccine. Laureth-9 low dose (0.1%) was
     ineffective in enhancing the boosting response to TT, contrary to the 0.5%
     dose. However, the adjuvanticity of that formulation was strongly
     improved by supplementing it with Triton X100. The antibody response
     elicited was similar to the one induced by the com. DTPa vaccine.
     9002-92-0, Polyethylene glycol lauryl ether 9002-93-1,
     Triton X100 9004-81-3, Polyethylene glycol laurate
     9005-00-9, Polyethylene glycol stearyl ether 9005-64-5,
     Tween 20 9005-65-6, Tween 80 9034-40-6, LRH
     9036-19-5, Octoxynol 25322-68-3D, alkyl ethers or esters
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
         (adjuvant comprising polyoxyethylene alkyl ether or
         ester and nonionic surfactant)
     9002-92-0 HCAPLUS
CN
     Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA
     INDEX NAME)
        -CH_2-CH_2-O-\frac{1}{n} (CH<sub>2</sub>)<sub>11</sub>-Me
     9002-93-1 HCAPLUS
RN
     Poly(oxy-1,2-ethanediyl), .alpha.-\{4-(1,1,3,3-tetramethylbutyl)phenyl\}-
     .omega.-hydroxy- (9CI) (CA INDEX NAME)
```

$$\begin{array}{c|c} \text{Me} & \\ \end{array}$$

RN 9004-81-3 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxododecyl)-.omega.-hydroxy- (9CI)
(CA INDEX NAME)

Me-
$$(CH_2)_{10}$$
 - C - CH_2 - CH

RN 9005-00-9 HCAPLUS CN Poly(oxy-1,2-ethanediyl), .alpha.-octadecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$HO - \begin{bmatrix} -CH_2 - CH_2 - O \end{bmatrix}_n (CH_2)_{17} - Me$$

RN 9005-64-5 HCAPLUS

CN Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9005-65-6 HCAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9034-40-6 HCAPLUS

CN Luteinizing hormone-releasing factor (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9036-19-5 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN

25322-68-3 HCAPLUS
Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX CN NAME)

$$HO = CH_2 - CH_2 - O = I$$

RN

199810-71-4 HCAPLUS DNA, d(T-C-C-A-T-G-A-C-G-T-T-C-C-T-G-A-C-G-T-T) (9CI) (CA INDEX NAME) CN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE *** RE.CNT 2

RE

- (1) Modi; WO 9636352 A 1996 HCAPLUS (2) Smithkline-Beecham; WO 9952549 A 1999 HCAPLUS

```
=> d bib abs hitstr 3
     ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS
L7
     1999:672602 HCAPLUS
AN
     131:309797
DN
ΤI
     Adjuvant compositions
     Friede, Martin; Hermand, Philippe
     Smithkline Beecham Biologicals S.A., Belg.
PA
     PCT Int. Appl., 52 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                                            APPLICATION NO. DATE
                      KIND DATE
PΙ
     WO 9952549
                       A1
                             19991021
                                            WO 1999-EP2278
                                                             19990329
         W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
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             JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
             MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9934197
                       A1
                             19991101
                                            AU 1999-34197
                                                              19990329
     BR 9909915
                             20001226
                                            BR 1999-9915
                                                              19990329
                       Α
                                            EP 1999-915735
     EP 1069910
                             20010124
                                                             19990329
                       A1
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI
     NO 2000005051
                             20001121
                                            NO 2000-5051
                                                              20001006
PRAI GB 1998-7805
                       Α
                             19980409
     GB 1998-20956
                             19980925
                       Α
     WO 1999-EP2278
                             19990329
                       W
     MARPAT 131:309797
OS
     The present invention relates to an adjuvant compn. comprising a
     polyoxyethylene ether or a polyoxyethylene ester, in
     combination with a pharmaceutically acceptable excipient, and to a vaccine
     comprising such adjuvant compns. and antigen. In addn., the
     present invention relates to the use of polyoxyethylene ethers
     or esters in the manuf. of adjuvant formulations, and vaccine
     formulations, and their use as medicaments.
     9034-40-6, Luteinizing hormone-releasing hormone
TΤ
     141256-04-4, QS21
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (adjuvant compns. comprising polyoxyethylene ether
        or ester for mucosal vaccine)
     9034-40-6 HCAPLUS
RN
CN
     Luteinizing hormone-releasing factor (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     141256-04-4 HCAPLUS
RN
     .beta.-D-Glucopyranosiduronic acid, (3.beta.,4.alpha.,16.alpha.)-28-[[O-D-
CN
     apio-.beta.-D-furanosyl-(1.fwdarw.3)-O-.beta.-D-xylopyranosyl-(1.fwdarw.4)-
     arabinofuranosyloxy)-3-hydroxy-6-methyl-1-oxooctyl]oxy]-3-hydroxy-6-methyl-
     1-oxooctyl]-6-deoxy-.beta.-D-galactopyranosyl]oxy]-16-hydroxy-23,28-
     dioxoolean-12-en-3-yl O-.beta.-D-galactopyranosyl-(1.fwdarw.2)-O-[.beta.-D-xylopyranosyl-(1.fwdarw.3)]- (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 1-C

PAGE 2-A

1,2,3-Propanetriol (9CI) (CA INDEX NAME)

 $\begin{array}{c} \text{OH} \\ \mid \\ \text{HO-CH}_2\text{-CH-CH}_2\text{-OH} \end{array}$

RN 106-08-1 HCAPLUS CN Dodecanoic acid, 26-hydroxy-3,6,9,12,15,18,21,24-octaoxahexacos-1-yl ester (9CI) (CA INDEX NAME)

PAGE 1-A

HO-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-

PAGE 1-B

RN 3055-99-0 HCAPLUS CN 3,6,9,12,15,18,21,24,27-Nonaoxanonatriacontan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

PAGE 1

 ${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-C$

PAGE 1-B

— ${\rm CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me}$

RN 5274-68-0 HCAPLUS CN 3,6,9,12-Tetraoxatetracosan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME) ${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me}$

RN 7300-85-8 HCAPLUS

CN 3,6,9,12,15,18,21,24,27-Nonaoxapentatetracontan-1-ol (9CI) (CA INDEX NAME)

PAGE 1-A

HO-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O

PAGE 1-B

— ${\rm CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{17}-Me}$

RN 9002-92-0 HCAPLUS

HO
$$-$$
 CH₂ - CH₂ - O $-$ (CH₂)₁₁ - Me

RN 9012-76-4 HCAPLUS

CN Chitosan (8CI, 9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 13149-87-6 HCAPLUS

CN 3,6,9,12,15,18,21,24-Octaoxadotetracontan-1-ol (7CI, 8CI, 9CI) (CA INDEX NAME)

PAGE 1-A

HO-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-O-CH2-CH2-O

PAGE 1-B

- CH2- CH2- O- CH2- CH2- O- CH2- CH2- O- (CH2) 17- Ме

RN 25322-68-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)

RN 26023-30-3 HCAPLUS

CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)

RN 26680-10-4 HCAPLUS 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, homopolymer (9CI) (CA INDEX NAME) CN CM CRN 95-96-5 CMF C6 H8 O4 CDES *

RN 26780-50-7 HCAPLUS 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione CN (9CI) (CA INDEX NAME)

CM 1

CRN 502-97-6 CMF C4 H4 O4

2 CM

CRN 95-96-5 CMF C6 H8 O4 CDES *

190977-41-4 HCAPLUS

DNA, d(P-thio)(T-C-T-C-C-A-G-C-G-T-G-C-G-C-C-A-T) (9CI) (CA INDEX NAME) CN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 202668-42-6 HCAPLUS

DNA, d(P-thio)(T-C-C-A-T-G-A-C-G-T-T-C-C-T-G-A-C-G-T-T) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 247116-67-2 HCAPLUS

DNA, d(P-thio)(T-C-C-A-T-G-A-G-C-T-T-C-C-T-G-A-C-G-T-T) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

192778-00-0, GenBank A90868 247214-44-4, PN: WO9952549 ΙT PAGE: 26 unclaimed DNA

RL: PRP (Properties)

(unclaimed nucleotide sequence; adjuvant compns.)
192778-00-0 HCAPLUS
GenBank A90868 (9CI) (CA INDEX NAME)

RN

CN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 247214-44-4 HCAPLUS

PN: WO9952549 PAGE: 26 unclaimed DNA (9CI) (CA INDEX NAME) CN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RE.CNT '6

RE

- (1) Carlson, A; US 3919411 A 1975 HCAPLUS (2) James, A; WO 9319781 A 1993 HCAPLUS (3) Lyfjathroun, H; WO 9417827 A 1994 HCAPLUS (4) Macdo, B; WO 9509651 A 1995 HCAPLUS (5) Micro Vesicular Systems; WO 8806882 A 1988 HCAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2001 ACS
L29
     2000:240985 HCAPLUS
AN
     132:292701
ΤI
     Novel methods for therapeutic vaccination
     Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious; Haaning,
IN
     Jesper: Leach, Dana; Dalum, Iben; Gautam, Anand; Birk, Peter; Karlsson,
     Gunilla
     M Amp E Biotech A/s, Den.
SO
     PCT Int. Appl., 220 pp.
     CODEN: PIXXD2
DΤ
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                       KIND DATE
                                             APPLICATION NO. DATE
                             20000413
PT
     WO 2000020027
                       A2
                                             WO 1999-DK525
                                                               19991005
     WO 2000020027
                        A3
                             20001012
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             LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK,
                                       SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                             20000426
     AU 9958510
                        A1
                                             AU 1999-58510
                                                               19991005
     EP 1117421
                        A2
                             20010725
                                              EP 1999-945967
                                                              19991005
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI,
             LT, LV, FI, RO
PRAI DK 1998-1261
                             19981005
                        Α
     US 1998-105011
                        ₽
                             19981020
     WO 1999-DK525
                        W
                             19991005
     A method is disclosed for inducing cell-mediated immunity against cellular
     antigens. More specifically, the invention provides for a method for
     inducing cytotoxic T-lymphocyte immunity against weak antigens, notably
     self-proteins. The method entails that antigen presenting cells are
     induced to present at least one CTL epitope of the weak antigen and at the
     same time presenting at least one foreign T-helper lymphocyte epitope. In
     a preferred embodiment, the antigen is a cancer specific antigen, e.g.
     prostate specific membrane antigen (PSM), Her2, or FGF8b. The method can
     be exercised by using traditional polypeptide vaccination, but also by
     using live attenuated vaccines or nucleic acid vaccination. The invention
     furthermore provides immunogenic analogs of PSM, Her2 and FGF8b, as well
     as nucleic acid mols. encoding these analogs. Also vectors and
     transformed cells are disclosed. The invention also provides for a method
     for identification of immunogenic analogs of weak or non-immunogenic
     antigens.
IT
     25322-68-3
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (adjuvant; weak antigens inserted with foreign T cell epitope
        as vaccines)
     25322-68-3 HCAPLUS
     Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX
     NAME)
      --- CH<sub>2</sub>-- CH<sub>2</sub>-- О
```

=> d ind

L29 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2001 ACS

IC A61K039-00

· · · · · · ·

```
15-2 (Immunochemistry)
CC
     Section cross-reference(s): 3, 63
ST
     weak antigen vaccine cytotoxic T lymphocyte; tumor antigen T cell epitope
     vaccine
IT
     Antigens
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (17-1A; weak antigens inserted with foreign T cell epitope as vaccines)
     Antigens
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (AM-1; weak antigens inserted with foreign T cell epitope as vaccines)
     Antigens
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (APC; weak antigens inserted with foreign T cell epitope as vaccines)
     Antigens
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (APRIL; weak antigens inserted with foreign T cell epitope as vaccines)
ΙT
     Antigens
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (BAGE; weak antigens inserted with foreign T cell epitope as vaccines)
     Chemokines
        (C-X-C, Ena78; weak antigens inserted with foreign T cell epitope as
        vaccines)
     CD antigens
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (CD33; weak antigens inserted with foreign T cell epitope as vaccines)
     Glycoproteins, specific or class
IΤ
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (CD40-L (antigen CD40 ligand); weak antigens inserted with foreign T
        cell epitope as vaccines)
ΙT
     Antigens
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (CD52; weak antigens inserted with foreign T cell epitope as vaccines)
     Antigens
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (CDC27; weak antigens inserted with foreign T cell epitope as vaccines)
ΙT
     Antigens
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (CO17-1A; weak antigens inserted with foreign T cell epitope as
        vaccines)
TΤ
     Antigens
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (CS (circumsporozoite), epitope; weak antigens inserted with foreign T
        cell epitope as vaccines)
     Proteins, specific or class
TΨ
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (DCC (deleted in colorectal cancer); weak antigens inserted with
        foreign T cell epitope as vaccines)
ΙT
     Antigens
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (DcR3; weak antigens inserted with foreign T cell epitope as vaccines)
     Proteins, specific or class
ΙT
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (E6; weak antigens inserted with foreign T cell epitope as vaccines)
     Transcription factors
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (E7; weak antigens inserted with foreign T cell epitope as vaccines)
     Hematopoietin receptors
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (FLT3 receptors; weak antigens inserted with foreign T cell epitope as
```

```
=> d bib abs hitstr 1
     ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN
     1999:215575 HCAPLUS
     130:247033
DN
     Synergistic composition and methods for treating neoplastic or cancerous
TΙ
     growths and for restoring or boosting hematopoiesis
     Hanna, Nabil; Braslawsky, Gary R.; Hariharan, Kandasamy
     Idec Pharmaceuticals Corporation, USA
PΑ
     PCT Int. Appl., 41 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                      KIND
                            DATE
                                            APPLICATION NO. DATE
     WO 9913912
                             19990325
                                            WO 1998-US18495
                                                             19980917
РΤ
                       A1
             AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                             19990330
                                            ZA 1998-8461
                                                              19980916
     ZA 9808461
                       Α
                            19990405
                                            AU 1998-95658
                                                              19980917
     AU 9895658
                       A1
     EP 1015031
                       A1
                             20000705
                                            EP 1998-949313
                                                             19980917
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
                                                              20000317
                             20000518
                                            NO 2000-1413
     NO 2000001413
                       Α
PRAI US 1997-933359
                             19970918
                       Α
     WO 1998-US18495
                       W
                             19980917
     A method for treating neoplastic or cancerous growths and for treating
     cancer patients to restore or boost hematopoiesis comprises administration
     of a combination of a cytotoxic T-lymphocyte (CTL)-inducing compn. and
     .gtoreq.1 agent capable of neutralizing or down-regulating the activity of
     tumor-secreted immunosuppressive factors such as TGF-.beta. and IL-10,
     sep. or in combination. The CTL inducer is typically a vaccine for
     enhancing tumor immunity which lacks an immunostimulating peptide
     component and is formulated as a stable oil-in-water emulsion contg. a
     micelle-forming agent. The combination produces a synergistic
     enhancement of the CTL response. Since TGF-.beta. neg. regulates and/or
     inhibits the growth of hematopoietic cells, the treatment can improve
     hematopoiesis during cancer therapy. Thus, mice bearing progressively
     growing ovalbumin-expressing EG7 tumors showed a delay in tumor growth
     after treatment with 30 .mu.g ovalbumin in Provax adjuvant and 50 .mu.g
     anti-TGF-.beta. antibodies.
     9005-64-5, Tween 20 9005-65-6, Tween 80
     25322-68-3, PEG
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (in vaccine adjuvant; synergistic compn. and methods for
        treating neoplastic or cancerous growths and for restoring or boosting
        hematopoiesis)
RN 
     9005-64-5 HCAPLUS
CN
     Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA
     INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN
     9005-65-6 HCAPLUS
     Sorbitan, mono-(92)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs.
CN
            (CA INDEX NAME)
     (9CI)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     25322-68-3 HCAPLUS
     Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX
     NAME)
```

$${\tt HO} \begin{array}{c|c} & {\tt CH_2-CH_2-O-J_n-H} \end{array}$$

RE.CNT 3 RE

- (1) Murphy; The Journal of Experimental Medicine 1993, V178, P231 HCAPLUS (2) Raychaudhuri; US 5585103 A 1996 HCAPLUS (3) Richards; Cell Immunol 1998, V184(2), P85 HCAPLUS

=> d bib abs hitstr 2

```
ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS
L30
AN
     1998:268384 HCAPLUS
DN
     Adjuvant, in particular as an emulsion, containing a trivalent metal
ΤI
     cation and sympathomimetic compound, and vaccine composition containing it
IN
     Ganne, Vincent; Aucouturier, Jerome
PA
     Societe D'Exploitation de Produits pour les Industries Chimiques SEPPIC,
so
     PCT Int. Appl., 26 pp.
     CODEN: PIXXD2
DT
     Patent
     French
LA
FAN.CNT 3
     PATENT NO.
                      KIND DATE
                                           APPLICATION NO. DATE
                            19980430
                                           WO 1997-FR1816
                                                            19971010
PΙ
     WO 9817311
                       A1
        W: BR, JP
        RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
                            19980424
                                           FR 1996-12718
                                                            19961018
     FR 2754715
                       A1
                       B1
                            19981113
     FR 2754715
     EP 939649
                       Α1
                            19990908
                                           EP 1997-909390
                                                            19971010
        R: BE, DE, ES, FR, GB, IT, NL
     BR 9712546
                            19991019
                                           BR 1997-12546
                                                            19971010
     JP 2000507610
                       т2
                            20000620
                                           JP 1998-519016
                                                            19971010
PRAI FR 1996-12718
                            19961018
                       Α
     WO 1997-FR1816
                       W
                            19971010
     A compn. is disclosed contg.: (i) .gtoreq.1 antigen or .gtoreq.1 in vivo
     generator of a compd. comprising an amino acid sequence; and (ii)
     .gtoreq.1 adjuvant. The adjuvant contains a salt of a trivalent metal
     cation and an org. anion, e.g. aluminum salicylate or aluminum acetate,
     and .gtoreq.1 sympathomimetic compd. The invention also concerns their
     use as medicine.
     25322-68-3D, fatty acid esters
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (surfactant; adjuvant emulsion, with trivalent metal cation
        and sympathomimetic compd., and vaccine compn. contg. it)
     25322-68-3 HCAPLUS
     Poly(oxy-1,2-ethanediy1), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX
```

NAME)

=> d kwic 2

- L30 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS
- Micelles

(soln.; adjuvant emulsion, with trivalent metal cation and sympathomimetic compd., and vaccine compn. contg. it) 50-70-4D, D-Glucitol, fatty acid esters 56-81-5D, 1,2,3-Propanetriol, IT

fatty acid esters 25322-68-3D, fatty acid esters
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surfactant; adjuvant emulsion, with trivalent metal cation and sympathomimetic compd., and vaccine compn. contg. it)

- ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
- 1998:127592 HCAPLUS AN
- DN 128:261743
- ΤI Elutability of proteins from aluminum-containing vaccine adjuvants by treatment with surfactants
- Rinella, Joseph V., Jr.; Workman, Ryan F.; Hermodson, Mark A.; White, Joe L.; Hem, Stanley L.
- Dep. Industrial and Physical Pharmacy, Chemistry, Biochemistry, and Agronomy, Purdue Univ., West Lafayette, IN, 47907, USA
 J. Colloid Interface Sci. (1998), 197(1), 48-56
 CODEN: JCISA5; ISSN: 0021-9797 CS
- SO
- PB Academic Press
- DTJournal
- LA English
- The elutability of proteins from adjuvants in model vaccines composed of ovalbumin adsorbed by aluminum hydroxide adjuvant or lysozyme adsorbed by aluminum phosphate adjuvant following treatment with surfactant solns. was studied. Nonionic (Triton X-100, lauryl maltoside), zwitterionic (lauryl sulfobetaine), anionic (sodium dodecyl sulfate), and cationic (cetylpyridinium chloride, dodecyltrimethylammonium chloride) surfactants were investigated. Cetylpyridinium chloride produced the greatest degree of elution (60%) of ovalbumin from aluminum hydroxide adjuvant. Sodium dodecyl sulfate completely eluted lysozyme from aluminum phosphate adjuvant. The effectiveness of surfactants in removing preadsorbed proteins was directly related to their ability to denature the protein. Micellar solubilization and electrostatic repulsion may also contribute to desorption.
- **9002-93-1**, Triton X-100
 - RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (elutability of proteins from aluminum-contg. vaccine adjuvants by treatment with surfactants)
- 9002-93-1 HCAPLUS RN
- Poly(oxy-1, 2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-CN .omega.-hydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \\ \text{Me} & \\ \text{Me} & \\ \text{Me} & \\ \end{array}$$

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=> d bib abs hitstr 4
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30 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:15525 HCAPLUS

DN 126:73781

TI Multiple antigenic peptide system having adjuvant properties for use in vaccines

IN Tam, James P.

PA Tam; James P., USA

SO U.S., 24 pp. Cont. of U.S. Ser. No. 877,613,abandoned.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
ΡI	JIS 5580 563	Α	19961203	•	US 1994-331489	19941228
	WO 9322343	A1	19931111		WO 1993-US4179	19930503
	W: CA, JP,	US				

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1992-877613 19920501 WO 1993-US4179 19930503

A multiple antigenic peptide system is disclosed that comprises a dendritic core and peptides and a lipophilic anchoring moiety. This peptide system is capable of eliciting an immune response when injected into a mammal; vaccines prepd. from the system and methods of use including therapeutic protocols are included. This combination eliminates the need for the inclusion of adjuvants found to be toxic to humans, and facilitates the exponential amplification of the antigenic potential of a vaccine prepd. therefrom, as noncovalent amplification by a liposome or micellar form is possible. Further, multiple different antigenic peptides may be attached so that the system may be prepd. for administration to concurrently treat diverse ailments, e.g. AIDS and Thus, 4 copies of a 24-residue peptide (designated B1) of the V3 loop of HIV-1 gp120 were linked to the free N.alpha. and N.epsilon. positions of N.alpha., N.epsilon.-dilysyl-Lys-Ser-Ser-[N.epsilon.-(tripalmitoyl-S-glycerylcysteinyl)]lysyl-alanine, and the product was incorporated into liposomes which were used to immunize mice. The immunized mice showed a high-titer humoral antibody response, a mitogenic response in spleen cells, a CD4+ T-helper cell response, a cytotoxic T-lymphocyte response, and formation of IL-2 by spleen cells after restimulation.

IT 25322-68-3D, conjugates with peptides
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(multiple antigenic peptide system having adjuvant properties
for use in vaccines)

for use in vaccines)
RN 25322-68-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$HO = \begin{bmatrix} CH_2 - CH_2 - O \end{bmatrix} \frac{1}{n} H$$

```
=> d bib abs hitstr 1
L33 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS
     2000:756545 HCAPLUS
AN
      133:340220
DN
ΤI
     Adjuvant comprising a saponin and an immunostimulatory oligonucleotide for
     manufacture of vaccines
TN
      Friede, Martin; Garcon, Nathalie; Hermand, Philippe
PA
     Smithkline Beecham Biologicals S. A., Belg.
      PCT Int. Appl., 52 pp.
      CODEN: PIXXD2
DΤ
     Patent
     English
T.A
FAN.CNT 1
      PATENT NO.
                        KIND DATE
                                                APPLICATION NO. DATE
PΙ
     WO 2000062800
                         A2
                               20001026
                                                WO 2000-EP2920
                                                                  20000404
     WO 2000062800
                               20010111
                         А3
          W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
              CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,
              IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
              SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,
              AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
              DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                        A 19990419
PRAI GB 1999-8885
     US 1999-301829
                               19990429
     The present invention relates to adjuvant compns. which are suitable to be
     used in vaccines. In particular, the adjuvant compns. of the present invention comprises a saponin and an immunostimulatory oligonucleotide,
     optionally with a carrier. Also provided by the present invention are
     vaccines comprising the adjuvants of the present invention and an antigen.
     Further provided are methods of manuf. of the adjuvants and vaccines of
     the present invention and their use as medicaments. Methods of treating
     an individual susceptible to or suffering from a disease by the
     administration of the vaccines of the present invention are also provided.
     9034-40-6, GNRH
     RL: BOC (Biological occurrence); PEP (Physical, engineering or chemical
     process); THU (Therapeutic use); BIOL (Biological study); OCCU
      (Occurrence); PROC (Process); USES (Uses)
         (adjuvant comprising a saponin and an immunostimulatory
         oligonucleotide for manuf. of vaccines)
     9034-40-6 HCAPLUS
     Luteinizing hormone-releasing factor (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
=> d kwic
L33 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS IT 11024-24-1, Digitonin 11072-93-8, .beta.-Escin
                                                             66594-14-7, Quil A
     141256-04-4, QS21 208933-54-4, QS7 218138-45-5, QS17
     RL: BAC (Biological activity or effector, except adverse); PEP (Physical,
     engineering or chemical process); THU (Therapeutic use); BIOL (Biological
      study); PROC (Process); USES (Uses)
         (adjuvant comprising a saponin and an immunostimulatory oligonucleotide
         for manuf. of vaccines)
     9002-10-2, Tyrosinase 9034-40-6, GNRH 226408-87-3, Prostase RL: BOC (Biological occurrence); PEP (Physical, engineering or chemical
     process); THU (Therapeutic use); BIOL (Biological study); OCCU
      (Occurrence); PROC (Process); USES (Uses)
         (adjuvant comprising a saponin and an immunostimulatory
         oligonucleotide for manuf. of vaccines)
```

```
ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS
     1999:166519 HCAPLUS
AN
     130:200945
DN
TΙ
     Compositions comprising the adjuvant QS-21 and polysorbate or cyclodextrin
     as excipient
IN
     Kensil, Charlotte; Beltz, Gerald A.
PA
     Aquila Biopharmaceuticals, Inc., USA
     PCT Int. Appl., 42 pp.
SO
     CODEN: PIXXD2
DТ
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                      KIND DATE
                                            APPLICATION NO.
                                                             DATE
     _____
                      ----
PΙ
    WO 9910008
                       A1
                            19990304
                                            WO 1998-US17940 19980828
             AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,
                                                              ТJ,
                                                                  TM,
                                                                      TR,
             UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9892107
                       A1
                            19990316
                                            AU 1998-92107
                                                             19980828
     AU 734180
                       В2
                            20010607
                            20000621
     EP 1009429
                       A1
                                            EP 1998-944600
                                                             19980828
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
PRAI US 1997-57255
                            19970829
                       Ρ
     WO 1998-US17940
                     W
                            19980828
     Certain novel compns. of the adjuvant saponin QS-21 having improved
     properties are disclosed. The compns. of the present invention are
     designed (1) to minimize the lytic effects of QS-21, (2) to improve the
     tolerance of QS-21 contg. formulations in humans or other animals, (3) to
     stabilize the QS-21 from alk. hydrolysis and/or (4) to maintain the high
     adjuvant potency of the QS-21 product. These compns. may be employed with
     vaccines comprising proteins or peptides, polysaccharides, lipids, or
     nucleic acids. Hydroxypropyl-.beta.-cyclodextrin minimized the lytic
     effect (increased the hemolytic index) of QS-21 and it hemolytic index was
     93 .mu.g/mL at 32 mg/mL.
    9002-93-1, Triton x100 9005-64-5, Polysorbate 20 9005-65-6, Polysorbate 80
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (compns. comprising adjuvant QS-21 and polysorbate or
        cyclodextrin as excipient)
RN
     9002-93-1 HCAPLUS
     Poly(oxy-1, 2-ethanediy1), .alpha.-[4-(1,1,3,3-tetramethylbuty1)pheny1]-
CN
     .omega.-hydroxy- (9CI) (CA INDEX NAME)
                        о— сн<sub>2</sub>— сн<sub>2</sub>-
Me3C-CH2
RN
     9005-64-5 HCAPLUS
CN
     Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA
     INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    9005-65-6 HCAPLUS
```

- Sorbitan, mono-(92)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)
- *** STRUCTURE DIAGRAM IS NOT AVAILABLE *** RE.CNT 9
- RE
- (1) Behringwerke Ag; EP 0187286 A 1986 HCAPLUS(2) Dr MaintsuKk; JP 06343419 A 1994 HCAPLUS
- (3) Gerber Jay, D; US 4806350 A 1989 HCAPLUS
- (4) Peptide Technology Ltd; WO 9104052 A 1991 HCAPLUS (5) Ralph, A; GB 1083815 A 1967 HCAPLUS ALL CITATIONS AVAILABLE IN THE RE FORMAT

cyclodextrin as excipient)

- => d kwic 2
- L33 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS
- adjuvant QS21 polysorbate cyclodextrin excipient ST
- 7585-39-9, beta.-Cyclodextrin 7585-39-9D, beta.-Cyclodextrin, hydroxypropyl ether 9002-93-1, Triton x100 9005-64-5, Polysorbate 20 9005-65-6, Polysorbate 80 9005-66-7, Polysorbate 40 9005-67-8, Polysorbate 60 10016-20-3, Polysorbate 60 10016-20-3, Polysorbate 60 10016-20-3, Polysorbate 60 10016-20-4, Polysorbate 60 1 .alpha.-Cyclodextrin 66594-14-7, Quil a 141256-04-4, QS-21 208933-54-4, QS-7 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compns. comprising adjuvant QS-21 and polysorbate or

```
=> d bib abs hitstr 3
    ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS
L33
     1999:7854 HCAPLUS
ΑN
DN
     130:57241
     Oil-in-water vaccine compositions
ΤI
     Garcon, Nathalie; Momin, Patricia Marie Christine Aline Francoise
IN
PA
     Smithkline Beecham Biologicals S.A., Belg.
     PCT Int. Appl., 30 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                       KIND DATE
                                             APPLICATION NO. DATE
PΙ
     WO 9056414
                        ΑI
                              19981217
                                             WO 1998-EP3479
                                                               19980603
         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, ML, MR, NE, SN, TD, TG
     AU 9883365
                        A1
                             19981230
                                             AU 1998-83365
                                                               19980603
     AU 728759
                             20010118
                        B2
     EP 999852
                        A1
                             20000517
                                             EP 1998-933600
                                                              19980603
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI
                             20000912
     BR 9810614
                        Α
                                             BR 1998-10614
                                                               19980603
     NO 9906133
                             20000126
                                             NO 1999-6133
                                                               19991210
                        Α
PRAI GB 1997-11990
                             19970611
                        Α
     WO 1998-EP3479
                        W
                             19980603
     The present invention relates to improved stable oil-in-water emulsions
     having an oil droplet diam. of substantially 300-600 nm comprising
     triglycerides, and their use as vaccine adjuvants.
     9005-65-6, Tween 80
     RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical
     process); THU (Therapeutic use); BIOL (Biological study); PROC
     (Process); USES (Uses)
        (oil-in-water emulsions as vaccine adjuvants)
     9005-65-6 HCAPLUS
RN
     Sorbitan, mono-(9Z)-9-
(9CI) (CA INDEX NAME)
                         -9-octadecenoate poly(oxy-1,2-ethanediyl) derivs.
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RE.CNT 4
RE
(1) Granoff, D; Infection and Immunity 1997, V65(5), P1710 HCAPLUS
(2) Ott, G; Vaccine 1995, V13(16), P1557 MEDLINE (3) Pharmos Corp; WO 9511700 A 1995 HCAPLUS
(4) Smithkline Beecham Biologicals; WO 9517210 A 1995 HCAPLUS
=> d kwic 3
L33 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS
     9005-65-6, Tween 80
     RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical
     process); THU (Therapeutic use); BIOL (Biological study); PROC
     (Process); USES (Uses)
        (oil-in-water emulsions as vaccine adjuvants)
     59-02-9, .alpha.-Tocopherol 111-02-4, Squalene
                                                           538-23-8, Tricaprylin
     128478-31-9, 3D-MPL
                           141256-04-4, QS 21
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (oil-in-water emulsions as vaccine adjuvants)
```

```
=> d bib abs hitstr
L36 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2001 ACS
     2000:240985 HCAPLUS
     132:292701
DN
     Novel methods for therapeutic vaccination
ΤI
IN
     Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious; Haaning,
     Jesper; Leach, Dana; Dalum, Iben; Gautam, Anand; Birk, Peter; Karlsson,
     Gunilla
PA
     M Amp E Biotech A/s, Den.
     PCT Int. Appl., 220 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
FAN.CNT 1
     PATENT NO.
                        KIND DATE
                                              APPLICATION NO. DATE
                              20000413
        2000020027
                        A2
                                              WO 1999-DK525
                                                                 19991005
     WO 2000020027
                        A3
                              20001012
         W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
              CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
              LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO,
              RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ,
              VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
              CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                        A1
     AU 9958510
                              20000426
                                              AU 1999-58510
                                                                 19991005
                        A2
                              20010725
                                              EP 1999-945967
     EP 1117421
                                                                 19991005
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI,
              LT, LV, FI, RO
                              19981005
PRAI DK 1998-1261
     US 1998-105011
                        Ρ
                              19981020
     WO 1999-DK525
                        W
                              19991005
     A method is disclosed for inducing cell-mediated immunity against cellular
     antigens. More specifically, the invention provides for a method for
     inducing cytotoxic T-lymphocyte immunity against weak antigens, notably
     self-proteins. The method entails that antigen presenting cells are
     induced to present at least one CTL epitope of the weak antigen and at the
     same time presenting at least one foreign T-helper lymphocyte epitope. In
     a preferred embodiment, the antigen is a cancer specific antigen, e.g.
     prostate specific membrane antigen (PSM), Her2, or FGF8b. The method can
     be exercised by using traditional polypeptide vaccination, but also by
     using live attenuated vaccines or nucleic acid vaccination. The invention
     furthermore provides immunogenic analogs of PSM, Her2 and FGF8b, as well
     as nucleic acid mols. encoding these analogs. Also vectors and
     transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogs of weak or non-immunogenic
     antigens.
     25322-68-3
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (adjuvant; weak antigens inserted with foreign T cell epitope
        as vaccines)
RN
     25322-68-3 HCAPLUS
     Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX
```

$$HO = \begin{bmatrix} CH_2 - CH_2 - O \end{bmatrix}_n H$$

```
=> d bib abs hitstr 1
L42 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2001 ACS AN 1998:334648 HCAPLUS
      129:66833
     Immune adjuvant comprising synthetic bilayer membrane Yamada, koji; Okumura, Shiro; Akao, Satoshi
ΤI
IN
PΑ
      Fukuoka Prefecture, Japan
SO
      Jpn. Kokai Tokkyo Koho, 6 pp.
      CODEN: JKXXAF
DT
      Patent
      Japanese
LA
FAN.CNT 1
      PATENT NO.
                         KIND DATE
                                                  APPLICATION NO.
                                                                      DATE
PI
AB
                                19980526
      JP 10139685
                          A2
                                                  JP 1996-314277
                                                                     19961111
    Synthetic bimol. membrane comprising amphoteric compd. is used for
     enhancing immune adjuvant in prepn. of antibody. Thus, immune adjuvant comprising ovalbumin and micelle of 12GP2 and 14GP2 were prepd.
      and used for raising anti-ovalbumin IgG.
    9005-64-5, Tween 20
      RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
      (Uses)
         (immune adjuvant comprising synthetic bimol. membrane)
      9005-64-5 HCAPLUS
      Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA
CN
      INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
```

=> d bib abs hitstr 2

ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2001 ACS L42

1988:73342 HCAPLUS 108:73342 ΑN

DN

Synergistic effect of detergents and aluminum phosphate on the humoral ΤI immune response to bacterial and viral membrane proteins

Tacelink, Tom: Beuvery, E. Coen; Evenberg, Dolf; Van Wezel, Toon L. Dep. Bact. Vaccines, Natl. Inst. Public Health Environ. Hyg. (RIVM), AU Bilthoven, 3720 BA, Neth.

Vaccine (1987), 5(4), 307-14 SO CODEN: VACCUE, ISSN: 0264-410X

DT Journal

English LA

The influence of detergents on the immunogenic activity of the major outer membrane protein of Neisseria gonorrhoeae was investigated. Most detergents tested enhanced the immune response. This effect was synergistic with the adjuvant activity of AlPO4. The combination of detergent and AlPO4 showed a stronger adjuvant activity than Freund's complete adjuvant. The adjuvant effect was only obsd. with protein prepns. with very low lipopolysaccharide content. The immunostimulating effect of detergents was also obsd. with meningococcal group C polysaccharide conjugated to a Haemophilus influenzae type b outer membrane protein and with the fusion protein of measles virus. The influence of some detergent parameters (crit. micelle concn., hydrophile-lipophile balance, and charge) was investigated.

9002-93-1, Triton X-100 9005-64-5, Tween 20 9005-65-6, Tween 80

RL: BIOL (Biological study)

(immune adjuvant activity of, aluminum phosphate synergism with, in response to bacterial and viral membrane proteins)

9002-93-1 HCAPLUS RN

Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

RN 9005-64-5 HCAPLUS

CN Sorbitan, monododecanoate, poly(oxy-1,2-ethanediy1) derivs. (9CI) (CA

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9005-65-6 HCAPLUS

CN Sorbitan, mono-(92)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

```
=> d bib abs hitstr 3
     ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2001 ACS
     1986:193210 HCAPLUS
AN
     104:193210
DN
TΙ
     Erodible matrix for sustained release bioactive composition
IN
     Snipes, Wallace C.
     Zetachron, Inc., USA
PCT Int. Appl., 31 pp.
PA
SO
     CODEN: PIXXD2
DТ
     Patent
LA
     English
FAN.CNT 2
     PATENT NO.
                      KIND DATE
                                            APPLICATION NO.
                                                              DATE
                             ----
     WO 8600802
·PI
                       A1
                             19860213
                                             WO 1985-US1349
                                                              19850717
         W: AU, JP, KP
         RW: BE, CH, DE, FR, GB, NL
     CA 1246448
                      A1 19881213
                                             CA 1985-486711
                                                              19850712
     AU 8546388
                       A1
                             19860225
                                             AU 1985-46388
                                                              19850717
     AU 573149
                       B2
                             19880526
     EP 190255
                       A1
                             19860813
                                             EP 1985-903908
                                                              19850717
     EP 190255
                       В1
                            19921111
         R: BE, CH, DE, FR, GB, LI, NL
     JP 61502759
                       т2
                            19861127
                                             JP 1985-503436
                                                              19850717
PRAI US 1984-633604
                             19840723
     WO 1985-US1349
                             19850717
     A sustained-release oral compn. erodable in ag. soln.
     comprises 5-95% by wt. of PEG (mol. wt. 1000-20,000) and 95-5% of an
     erosion rate modifier (e.g., fatty acid) which is amphiphilic and insol.
     in the aq. soln. Thus, compns. contg. PEGs 1000,
     4000, 8000, or 20,000 (37.5% each), myristic acid 15%, starch (22.5%), and
     indomethacin 25% all released the drug gradually over a period of several
TТ
     25322-68-3
     RL: USES (Uses)
        (molding adjuvant, for sustained-release pharmaceuticals with
     polyethylene glycol matrix)
25322-68-3 HCAPLUS
RN
     Poly(oxy-1,2-ethanediy1), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX
CN
     NAME)
```

$$HO \longrightarrow CH_2 - CH_2 - O \longrightarrow n$$

=> d kwic 3

ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2001 ACS

AB A sustained-release oral compn. erodable in aq. soln.
comprises 5-95% by wt. of PEG (mol. wt. 1000-20,000) and 95-5% of an
erosion rate modifier (e.g., fatty acid) which is amphiphilic and insol.
in the aq. soln. Thus, compns. contg. PEGs 1000,
4000, 8000, or 20,000 (37.5% each), myristic acid 15%, starch (22.5%), and
indomethacin 25% all. . .

IT 25322-68-3
RL: USES (Uses)
(molding adjuvant, for sustained-release pharmaceuticals with
polyethylene glycol matrix)

=> d bib abs hitstr 4

```
L42 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2001 ACS AN 1984:169856 HCAPLUS
```

DN 100:169856

 ${\tt TI}$ Surface tension and contact angle of herbicide solutions affected by surfactants

AU Singh, Megh; Orsenigo, J. R.; Shah, D. O.

CS Inst. Food Agric. Sci., Univ. Florida, Lake Alfred, FL, 33850, USA

SO JAOCS, J. Am. Oil Chem. Soc. (1984), 61(3), 596-600 CODEN: JJASDH

DT Journal

LA English

GI

Contact angle and surface tension were measured for distd. H2O and hard water solns. of adjuvants Ortho X-77 [12687-90-0], Span-20 [1338-39-2], Sterox-NJ [59644-67-6], Surfactant-WK [60828-78-6], Triton B-1956, Triton X-114 [9036-19-5], Tween-20 [9005-64-5], and Sun Oil 11E. The same parameters were measured for suspensions of atrazine (I) [1912-24-9] and ametryn [834-12-8] with and without each adjuvant. All adjuvants reduced surface tension and contact angle of H2O; surfactant-WK was most effective and Tween-20 was least effective. Increasing concn. of surfactants from 0 to 0.1% (vol./vol.) gave progressive redn. in surface tension and contact angle, whereas higher concns., 0.1-2.0% (vol./vol.), had no further effect. Surfactant-WK at 0.1% in H2O reduced surface tension from 72.8 to 27 dynes/cm and contact angle from 110.degree. to 41.degree.. An addnl. increase in Surfactant-WK concn. from 0.1 to 2% did not further reduce surface tension and contact angle. Sun Oil 11E was identical in behavior except that it was less effective than the surfactants. Water hardness .ltoreq.1000 ppm as Ca2+ did not affect surface tension and contact angle in surfactant solns. An **aq. soln**. of I had a higher surface tension and contact angle than ametryn in the absence of surfactants. However, these differences were not obsd. when surfactants were added to either herbicide.

- L42 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2001 ACS
- 1984:73858 HCAPLUS
- 100:73858 DN
- Effect of pharmaceutical adjuvants on the rectal permeability of drugs. ΤI III. Effect of repeated administration and recovery of the permeability

- Nakanishi, Kunio; Masada, Mikio; Nadai, Tanekazu Fac. Pharm. Sci., Josai Univ., Sakado, 350-02, Japan Chem. Pharm. Bull. (1983), 31(11), 4161-6 CODEN: CPBTAL; ISSN: 0009-2363
- DТ Journal
- LA English
- Aq. solns. of Na deoxycholate [302-95-4], Na lauryl sulfate [151-21-3], di-Na ethylenediaminetetraacetate [139-33-3], and polyethylene glycol 400 [25322-68-3] were repeatedly perfused in the rectal lumen of rats. The epithelial cells affected by the adjuvants returned to the normal state within 2 h after the pretreatment. However, the goblet cells did not show complete recovery even at 24 h after the pretreatment, and the permeability of the membrane was still higher than the control value at that time. The permeability of the membrane on repeated treatment with the adjuvants was not increased as much as on the first treatment.

- L42 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2001 ACS
- AN 1977:429028 HCAPLUS
- 87:29028 DN
- Composition with immunostimulant action TI
- Renoux, Marie Louis; De Montis, Guy; Roche, Alain Laboratoires Crinex, Fr. IN
- PΑ
- Fr. Demande, 9 pp.
- CODEN: FRXXBL
- DΤ Patent
- T.A French

		-	-	~		_	-
FAN.	C	N	Т		1		

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
ΡI	FR 2306684	A1	19761105	FR 1975-11437	19750411	
	FR 2306684	B1	19800208			
AB	Immunostimulant	compns	. comprise pro	pylene glycol [57-	55-6], a surfactar	
glycerin [56-81-5], and a preservative in a buffered aq.						
	eoln For example an immunostimulant compn was prend					

- ınt, soln. For example, an immunostimulant compn. was prepd.
 comprising propylene glycol 9.83, glycerin 30, Tween 80 [9005-65-6] 6.66,
 sorbic acid 0.18 vitamin A [11103-57-4] 0.33 g, and pH 5 buffer soln., q.s.p. 100 mL.
- 9005-65-6
- RL: BIOL (Biological study)
 - (in immune adjuvant compn.)
- RN 9005-65-6 HCAPLUS
- Sorbitan, mono-(92)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)
- *** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

- ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2001 ACS
- 1973:47733 HCAPLUS AN
- 78:47733 DN
- Influence of auxiliary material on pharmaceuticals. 21. Mechanism of ΤI interaction between esters of nicotinic acid and poly(oxyethylene) ethers
- Ullmann, E.; Thoma, K.; Lippold, B. C. Inst. Pharm. Lebensmittelchem., Univ. Muenchen, Munich, Ger. CS
- Arch. Pharm. (Weinheim, Ger.) (1972), 305(11), 797-802 CODEN: ARPMAS
- DТ Journal
- German LA
- The interactions between surface-active poly(oxyethylene) ethers and esters of nicotinic acid take place in the hydrophobic interior and in the hydrophilic exterior of the ${\tt micelles}$. The degree of binding of the esters to the micelles depends particularly on the physicochem. properties of the esters. The lipophilic hexyl ester, e.g., is bound to a much greater extent than the hydrophilic Et ester. The structure of the surface-active agents has only a small effect. From the exptl. results, conclusions are drawn about the localization of the esters in the micelles.
- 9002-92-0 9005-00-9
 - RL: BIOL (Biological study)
- (pharmaceutical adjuvants, nicotinates reaction with)
- RN9002-92-0 HCAPLUS
- Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) INDEX NAME)

$$HO = \begin{bmatrix} -CH_2 - CH_2 - O \end{bmatrix}_n (CH_2)_{11} - Me$$

- 9005-00-9 HCAPLUS RN
- Poly(oxy-1,2-ethanediyl), .alpha.-octadecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$HO = \begin{bmatrix} CH_2 - CH_2 - O \end{bmatrix}_n (CH_2)_{17} - Me$$

- L42 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2001 ACS
- AN 1972:429091 HCAPLUS
- DN 77:29091
- TI Adsorption of drugs from the skeletal muscle of the rats. 3. Effect of water-soluble adjuvants and vehicles on intramuscular absorption
- AU Kakemi, Kiichiro; Sezaki, Hitoshi; Okumura, Katsuhiko; Kobayashi, Hiroshi; Furusawa, Shunji
- CS Fac. Pharm. Sci., Kyoto Univ., Kyoto, Japan
- SO Chem. Pharm. Bull. (1972), 20(3), 443-51 CODEN: CPBTAL
- DT Journal
- LA English
- AB The effects of the viscosity and osmotic pressure on the absorption mechanism of isonicotinamide [1453-82-3] and methylisonicotinate [2459-09-8] in the presence of adjuvants such as propylene glycol [57-55-6], glycerol [56-81-5], dextran [9004-54-0], polyethylene glycol [25322-68-3], and methyl cellulose [9004-67-5] were studied. From comparison of in vivo i.m. absorption studies in rats with in vitro diffusion expts. it was detd. that the injected soln. was absorbed from the injected site through the muscle fiber space and then the pores of the capillary walls. The latter step may be the rate limiting step in the absorptive process. The absorption mechanism of a drug with water-sol. adjuvants did not differ from that in aqueous soln. without any adjuvant. With small mol. wt. adjuvants such as propylene glycol or glycerol there was a correlation between the parenteral absorption rate and the reciprocal of viscosity of an injectable soln.

- L42 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2001 ACS
- AN 1972:94653 HCAPLUS
- DN 76:94653
- TI Biopharmaceutical studies on the effect of adjuvants on the absorption of drugs from drug formulations. 2. Intestinal absorption of sodium p-aminosalicylate from aqueous solutions in the presence of surface-active and macromolecular adjuvants
- AU Korossyova, Z.; Zathurecky, L.
- CS Inst. Exp. Pharmacol., Slovak. Acad. Sci., Bratislava, Czech.
- SO Pharmazie (1971), 26(11), 682-5 CODEN: PHARAT
- DT Journal
- LA German
- AB The surface-active agents Na lauryl sulfate [151-21-3], Septonex [10567-02-9], Tween 80 [9005-65-6], sucrose monolaurate [25339-99-5], sucrose monopalmitate [26446-38-8], and sucrose monostearate [25168-73-4] in concns. below the crit. micellar concn., when administered to rats by stomach bound together with Na p-aminosalicylate (I) [133-10-8] (0.01g/100g as 1% soln.), considerably (up to 2-fold) increased the absorption of I. Max. blood levels of I were reached 30 mins after administration both with and without the adjuvants. At concns. above the crit. micellar concn., these substances had less effect on I absorption. Me cellulose [9004-67-5] and gum arabic slightly increased but also delayed I absorption, due to their high viscosity.

=> d bib abs hitstr 10

- L42 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2001 ACS
- AN 1971:480281 HCAPLUS
- DN 75:80281
- TI Free-flowing, easily wettable particles containing acetylsalicylic acid
- IN Boncey, Graham A.; Hedge, Marice J.; Henderson, James Rae
- PA Aspro-Nicholas Ltd.
- GO Ger. Offen., 25 pp.
- CODEN: GWXXBX
- DT Patent
- LA German
- FAN.CNT 1

FAN.	PATENT NO.	KIND	DATE	AP	PLICATION NO.	DATE
PI	DE 2058434 DE 2058434	A B2	19710603 19800424	DE	1970-2058434	19701127
	DE 2058434	C3	19801218			
	GB 1287475	A	19720831	GB	1969-58203	19691128
	ZA 7007915	A	19710825	ZA	1970-7915	19701123
	US 3882228	Α	19750506		1970-92284	19701123
	IL 35714	A1	19740314		1970-35714	19701124
	IN 129401	A	19750816		1970-129401	19701126
	NL 7017417	A	19710602	NL	1970-17417	19701127
	NL 165928	В	19810115			
	NL 165928	С	19810615			
	FR 2073431	A5	19711001	FR	1970-42668	19701127
	FR 2073431	В1	19740322			
	AT 302533	В	19721025		1970-10713	19701127
	ES 385974	, A1	19730501		1970-385974	19701127
	CA 948108	A1	19740528		1970-99296	19701127
	DK 130453	В	19750224		1970-6054	19701127
	SE 383099	В	19760301		1970-16129	19701127
	JP 51006727	B4	19760302		1970-105390	19701128
	US 3887700	Α	19750603	US	1973-415247	19731112
PRAI			19691128			
	US 1970-92284		19701123			

AB The title prepn. consists of acetylsalicylic acid particles coated with one or more of the following compds. m. >105.degree.. low mol. wt. amino acids (glycine, methionine), sugars (sucrose, lactose, sugar polymers), sugar alcs. (mannitol, inositol, sorbitol) or mixts. thereof. In addn., the coat contains a wetting agent (cationic, anionic, nonionic types) and (or) a film-forming agent [gums, cellulose derivs., poly(vinylpyrrolidone)]. The ratio of acetylsalicylic acid to the total coating material is preferably between 7.1 to 1.1. Thus, the acetylsalicylic acid is suspended in an aq. soln. of the wetting agent. The suspension is treated with a small portion of an aq. soln. of the coating material and film-forming agent to form a thin paste. After the remaining soln. of coating material and film-forming agent is added, the suspension obtained is stirred continuously and spray-dried to small particles of which 95% should have a particle size <105 .mu. Thus coated acetylsalicylic acid particles may be made into water sol. powder or tablets or into effervescent powder or tablets. Six examples are given.

IT 9005-64-5

RL: BIOL (Biological study)

(pharmaceutical adjuvant, in coated powders)

RN 9005-64-5 HCAPLUS

CN Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)

^{***} STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d bib abs hitstr 1

- L48 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- AN 2001:108117 HCAPLUS
- DN 134:130980
- TI Preparation of chloride-free organic potassium-enriched compound fertilizer
- IN Zhang, Xiaochuan
- PA Peop. Rep. China
- SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
- CODEN: CNXXEV
- DT Patent
- LA Chinese
- FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1261065	Α	20000726	CN 2000-101170	20000127

The chem. component of the fertilizer comprises N 0-20, P (P205) 0-10, K (K20) 40-25, Zn 0.05-0.01, Fe 0-0.05, Mn 0-0.05, Mo 0-0.05, B 0-0.5, Ti 0-0.005%, and addnl. water and adjuvant. The adjuvant is a aq. soln. contg. surfactant 5-20 part and penetrating agent 5-20 part. The org. acids which form org. salt are selected from citric acid, levulinic acid, hydroxyacetic acid, malic acid, lactic acid, hydroxybutyric acid, maleic acid, oxalic acid, malonic acid, succinic acid, adipic acid, naphthenic acid, lauric acid, etc.; the surfactant from Na lignosulfonate, triacontanol, fatty alc. polyoxyethylene ether, CNF, MF, or WA; and the penetrating agent from JFC or M. The process comprises hydrolyzing furfural or 2-furylcarinol in one or two of org. acid, adding KOH or K2CO3, allowing to react to obtain K salt, adding one or more of borate, carbonate, hydroxide, silicate, phosphate, molybdate and sulfate of Zn, Fe, Cu, Mn, Mg and Ti, adjusting pH to 6-8, adding adjuvant, and mixing. The fertilizer can be absorbed by plant leaf or root, and accelerate plant growth.

=> d bib abs hitstr 2

- ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- 2001:84475 HCAPLUS AN
- DN 134:183476
- TΙ Oral antibacterial pharmaceutical formulation and method of its preparation
- Winiarski, Jerzy; Prosciewicz, Boguslaw; Pankowski, Jacek; Korda, Anna; Mroz, Anna; Lewandowska, Maria Bozena; Nowakowska, Krystyna; Wdowiarek, Włodzimierz; Gwozdz, Ewa; Ryll, Dorota; Kasiak, Irena Polska Akademia Nauk, Instytut Chemii Organicznej, Pol.; Tarchominskie
- PA Zaklady Farmaceutyczne POLFA S.A.
- Pol., 6 pp. CODEN: POXXA7
- DT Patent
- LA Polish
- FAN.CNT 1

KIND DATE APPLICATION NO. DATE PATENT NO. 20000331 PL 1995-307007

PI PL 178281 В1 19950131 The active antibacterial ingredient of the oral formulation is AB pivaloxymethyl ester of Z,7[2(2-aminothiazolyl-4)-2-methoxyimino]-3'deacetoxycephalosporinic acid in free form in amts. of 30-70 wt.%. The active ingredient is prepd. from Na salt of Z,7[2(2-aminothiazoly1-4)-2methoxyimino]-3'-deacetoxycephalosporinic acid in chilled (<5.degree.C) DMF in the presence of triethylamine and pivaloyloxymethyl iodide. After addn. of methanolic soln. of thiourea the reaction mixt. is slowly added to the aq. soln. of NaHCO3 and Na2S2O3 and formed ppt. is recovered, washed, and dried. The formulation is made with 30-70 wt.% of adjuvant ingredients (starch, Na starch glycolate, microcryst. cellulose, hydroxypropylcellulose derivs., polyethylene glycol, colloidal silica, Mg stearate, TiO2). The active ingredient is coated with a polyoxyethylene surface-active agent (SDS, Tween 80, <5 wt.%) in a solvent that does not dissolve the ester (water). When a homogeneous mixt. with the adjuvant ingredients is achieved, appropriate moisture level is adjusted by drying prior to capsule or tablet making. The capsules and tablets made with the surface-active agent showed accelerated rise in blood serum levels of the active ingredient in free acid form as detd. in 12 humans.

=> d bib abs hitstr 3

- ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- 2000:311828 HCAPLUS AN
- DN 133:271443
- Aqueous formulation of adjuvant-active nonionic block copolymers TΙ
- ΑU Todd, Charles W.; Newman, Mark J.
- CS
- Vaxcel, Inc., Norcross, GA, USA Methods Mol. Med. (2000), 42(Vaccine Adjuvants), 121-136 CODEN: MMMEFN
- Humana Press Inc. PΒ
- DT Journal; General Review
- LA English
- A review, with 22 refs., on adjuvant-active nonionic block copolymers that are flexible, linear structures with a core of a hydrophobic polyoxypropylene flanked on both ends by hydrophilic polyoxyethylene. Prepn. of copolymer soln. and formulations, dosing and applications, and safety are discussed.

RE.CNT 22

RE

- (4) Hem, S; Vaccine Design: The subunit and adjuvant approach 1995, P249 HCAPLUS
- (6) Hunter, R; J Immunol 1984, V133, P3167 HCAPLUS(9) Kensil, C; Vaccine Design: The subunit and adjuvant approach 1995, P525 HCAPLUS
- (11) Manetti, R; J Exp Med 1993, V177, P1199 HCAPLUS
- (12) Newman, M; Critical Rev Therap Drug Carrier Sys 1998, V15, P89 HCAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

- ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- 1998:532142 HCAPLUS
- DN 129:265225
- Design and Development of Adjuvant-Active Nonionic Block Copolymers ΤI
- Newman, Mark J.; Todd, Charles W.; Balusubramanian, Mannersamy Vaxcel Inc., Norcross, GA, 30092, USA
 J. Pharm. Sci. (1998), 87(11), 1357-1362 ΑU
- CS
- CODEN: JPMSAE; ISSN: 0022-3549 PB American Chemical Society
- DTJournal
- LA English
- Nonionic block copolymers are surfactants synthesized using propylene oxide and ethylene oxide, and they can be designed so that individual copolymers have unique vaccine adjuvant properties. We have designed and produced nonionic block copolymers based on high mol. wt. (MW), 9-15 kDA, cores of polyoxypropylene (POP) coupled with smaller polyoxyethylene (POE) end blocks. Copolymers synthesized with <10% POE will spontaneously assemble into 300 nm-3 .mu.m micelles or microparticles in aq. solns. at physiol. pH, and when formulated with protein, complex microparticles consisting of both the protein and copolymers are formed. The adjuvant activity of nonionic block copolymers is influenced by both size and POE content; maximal activity is assocd. with low POE content, 5-10%, and a mol. size of 11-12 kDa. The type of immune response produced is also influenced by the POE content. Copolymers with 10% POE significantly augmented Type 2 helper T-lymphocyte responses, whereas copolymers with lower POE contents augmented both Type 1 and Type 2 helper T-lymphocyte responses. This property allows for vaccines to be "customized" by using adjuvant-active nonionic block copolymers that will augment the most appropriate types of immune responses.

- ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- 1997:359440 HCAPLUS AN
- 127:55718 DN
- Development of an adjuvant-active nonionic block copolymer for use in TΙ oil-free subunit vaccine formulations
- Todd, C. W.; Pozzi, L.-A. M.; Guarnaccia, J. R.; Balasubramanian, M.; Henk, W. G.; Younger, L. E.; Newman, M. J.
- CS
- Vaxcel Inc., Norcross, GA, 30092, USA Vaccine (1997), 15(5), 564-570 SO CODEN: VACCDE; ISSN: 0264-410X
- PB Elsevier
- Journal DT
- LA English
- Nonionic block copolymers, synthesized from repeating units of ΑB oxypropylene and oxyethylene, can be designed so that individual copolymers have unique phys. properties with differential levels of adjuvant activity. The authors designed high mol. wt. block copolymers that spontaneously assemble into 500 nm-3 .mu.m particles when formulated with protein antigens in aq. solns. at physiol. pH. The adjuvant activity of one of these copolymers, termed CRL 1005, was compared to selected research adjuvants using ovalbumin (OVA) as the prototype vaccine antigen. Suboptimal doses of OVA were formulated with complete and incomplete Freund's adjuvant (CFA/IFA), alum, Quil-A saponins, Ribi Adjuvant System (RAS) or the CRL 1005 copolymer and these formulations were used to immunize C57BL/6 mice. The CRL1005 copolymer appeared to be more potent than either Quil-A or alum and comparable to the RAS formation, based on the nos. of responding mice and the OVA-specific antibody titers. Alum, RAS and Quil-A all augmented the prodn. of IgG1 and IgG2b similarly, whereas only the CFA/IFA boosted IgG2.alpha. levels significantly. The effect of adjuvants on relative antibody affinity was more variable with the CRL 1005 and CFA/IFA inducing antibodies with the highest affinity scores. This high mol. wt. nonionic copolymer is nontoxic in aq. formulations and should therefore by compatible with a wide variety of protein or polysaccharide vaccine

- L48 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- AN 1994:2671 HCAPLUS
- DN 120:2671
- $\mbox{{\bf TI}}$ $\mbox{{\bf Use}}$ and mode of action of adjuvants for herbicides: a review of some current work
- AU Kirkwood, Ralph C.
- CS Dep. Biosci. Biotechnol., Univ. Strathclyde, Glasgow, G4 ONR, UK
- SO Pestic. Sci. (1993), 38(2-3), 93-102 CODEN: PSSCBG; ISSN: 0031-613X
- DT Journal; General Review
- LA English
- A review with 90 refs. The use of surfactants, mineral and vegetable oils, emulsifiers and fertilizer salts, such as ammonium sulfate, can greatly enhance the activity of foliage-applied herbicides. Adjuvant herbicide interactions are reviewed with particular ref. to the benefits, including dose redn., enhanced and more consistent herbicide activity, and the nature of underlying mechanisms' the use and role of surfactants receive particular attention. Surfactants are used as activators in com. formulations of many herbicides to improve their foliar absorption and ultimate biol. activity. Current views on their influence are considered in relation to surface phenomena, solubilization of non-polar active ingredients, wax dissoln., cuticle penetration, preferential sites of penetration, membrane permeability and possible systemicity. The importance of a no. of moderating factors (plant, chem. and environmental) is discussed in the light of current work, with particular regard to herbicide polarity, surfactant type, Hydrophile-Lipophile Balance and crit. micelle concn. Current studies on the influence of nonionic polyoxyethylene surfactants of differing ethylene oxide (EO) content have underlined the importance of EO no. to their activity.

=> d bib abs hitstr 7

- ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- 1993:511266 HCAPLUS ΑN
- DN 119:111266
- TТ Development of a predictive uptake model to rationalize selection of polyoxyethylene surfactant adjuvants for foliage-applied agrochemicals
- ΑU Stock, David; Holloway, Peter J.; Grayson, B. Terence; Whitehouse, Paul
- Dep. Agric. Sci., Univ. Bristol, Bristol, BS18 9AF, UK Pestic. Sci. (1993), 37(3), 233-45 CS
- SO CODEN: PSSCBG; ISSN: 0031-613X
- DΤ Journal
- LA
- English AB Compn.-concn. relationships between a series of C13/C14 polyoxyethylene primary alc. (AE) surfactants and the foliar uptake enhancement of five model neutral org. compds. were examd. in factorially designed expts. on wheat (Triticum aestivum L.) and field bean (Vicia faba L.) plants grown under controlled environment conditions. Model compds. were applied to leaves as c.0.2-.mu.L droplets of 0.5 g/L solns. in aq . acetone in the absence or presence of surfactants at 0.2, 1 and 5 g/L. Uptake of the highly water-sol. compd., methylglucose (log octanol-water partition coeff. (P) = -3.0) was best enhanced by surfactants with high E (ethylene oxide) contents (AE15, AE20), whereas those of the lipophilic compds., WL110547 (log P=3.5) and permethrin (log P=6.5), were increased more by surfactants of lower E contents, esp. AE6. However, there was little difference between AE6, AE11, AE15 and AE20 in their ability to promote uptake of the two model compds. of intermediate polarity, phenylurea (log P = 0.8) and cyanazine (log P = 2.1). Abs. amts. of compd. uptake were also influenced strongly by both surfactant concn. and plant species. Greatest amts. of uptake enhancement were often obsd. at high surfactant concn. (5 g L) and on the waxy wheat leaves compared with the less waxy field bean leaves. The latter needed higher surfactant thresholds to produce significant improvements in uptake. Data from the expts. were used to construct a simple response surface model relating uptake enhancement to the E content of the surfactant added and to the physicochem. properties of the compd. to be taken up. Qual. predictions from this model might be useful in rationalizing the design of agrochem. formulations.

=> d kwic 7

- ANSWER 7 OF 13 | HCAPLUS | COPYRIGHT 2001 ACS L48
- Development of a predictive uptake model to rationalize selection of polyoxyethylene surfactant adjuvants for foliage-applied agrochemicals
- . faba L.) plants grown under controlled environment conditions. Model compds. were applied to leaves as c.0.2-.mu.L droplets of 0.5 g/L solns. in aq. acetone in the absence or presence of surfactants at 0.2, 1 and 5 g/L. Uptake of the highly water-sol. compd.,.

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=> d bib abs hitstr 9
    ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2001 ACS
L48
    1989:227175 HCAPLUS
AΝ
DN
    110:227175
ΤI
     Sustained-release microcapsules containing insecticidal toxins and drugs
    Speaker, Tycho J.; Collett, John H.; Chang, Frank N.; Harvey, William R.;
IN
     Speaker, Tully J.
PA
    Temple University, USA
SO
    Eur. Pat. Appl., 17 pp.
    CODEN: EPXXDW
    Patent
    English
LA
FAN.CNT 4
    PATENT NO.
                     KIND DATE
                                         APPLICATION NO. DATE
                           _____
    EP 299205
                     A1 19890118
                                         EP 1988-109276 19880610
    EP 299205
                     В1
                          19920415
        R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE
    US 4797234 A 19890110
                                         US 1987-64859 19870619
    US 4743583
                          19880510
                                         US 1987-75092
                                                         19870720
PRAI US 1987-64820
                          19870619
    US 1987-64821
                           19870619
```

AB Sustained-release microcapsules comprise a permeable anisotropic salt film encapsulating a proteinaceous biol. active core. The film is the reaction product of a Lewis base or salt thereof, in a slightly polar org. solvent, with a polyfunctional partially hydrophilic, partially lipophilic Lewis acid or salt thereof in aq. soln. or suspension. Adjuvants may be optionally present. The slightly polar org. solvent is a nondenaturing solvent or solvent complex capable of solubilizing or suspending the proteinaceous material. An aq. soln.

(10 mL) contg. 1 g arabic acid was stirred with a soln. of anhyd. piperazine (amt. stoichiometrically equiv. with arabic acid) and 0.005 g somatotropic hormone in butyrolactone (10 mL soln.), to give, after centrifuging, microcapsules.

19870619

19870720

=> d kwic 9

US 1987-64859

US 1987-75092

- L48 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- AB . . . thereof, in a slightly polar org. solvent, with a polyfunctional partially hydrophilic, partially lipophilic Lewis acid or salt thereof in aq. soln. or suspension. Adjuvants may be optionally present. The slightly polar org. solvent is a nondenaturing solvent or solvent complex capable of solubilizing or suspending the proteinaceous material. An aq. soln. (10 mL) contg. 1 g arabic acid was stirred with a soln. of anhyd. piperazine (amt. stoichiometrically equiv. with arabic. . .
- IT 107-15-3, Ethylenediamine, biological studies 9003-01-4D, crosslinked with polyalkenyl ethers 9003-11-6, Polyoxyethylene -polyoxypropylene 106392-12-5, Polyoxyethylene -polyoxypropylene block copolymer RL: BIOL (Biological study)
 - (as microencapsulation adjuvant, for insecticidal toxins and drugs)

- L48 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- 1986:83712 HCAPLUS ΑN
- 104:83712 DN
- ΤI The effect of adjuvants and oil carriers on photodecomposition of 2,4-D, bentazon, and haloxyfop
- ΑU
- Harrison, S. Kent; Wax, Loyd M.
 Dep. Agron., Univ. Illinois, Urbana, IL, 61801, USA
 Weed Sci. (1986), 34(1), 81-7 CS
- CODEN: WEESA6; ISSN: 0043-1745
- DT
- LA English
- Lab. photolysis rates of 2,4-D [94-75-7], bentazon [25057-89-0], and AΒ haloxyfop [69806-34-4] in dil. aq. soln. were enhanced by adjuvants. Addn. (vol./vol.) of 1.0% petroleum oil conc., 1.0% soybean oil conc., and 0.15% emulsifier package enhanced herbicide photolysis rates more than addn. of 0.15% oxysorbic [9005-64-5] (20 POE) (polyoxyethylene sorbitan monolaurate). Bioassays showed that phytotoxicity of photolyzed herbicide solns. was neg. correlated with time of exposure to UV light. Addn. of 0.85% acetophenone [98-86-2] to aq. herbicide solns. contg. 0.15% oxysorbic strongly sensitized photodegrdn. of 2,4-D, and to a lesser extent, haloxyfop. Acetophenone had no effect on bentazon photolysis in the presence of oxysorbic. In another study, herbicides were dissolved in white mineral oil or once-refined soybean oil and exposed to UV light. After a 6-h exposure, there was 92% loss of haloxyfop in mineral oil and 36% loss in soybean oil. There was no difference between oils in affecting the photolysis rate of 2,4-D or bentazon.

=> d bib abs hitstr 11

- L48 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- AN 1969:94799 HCAPLUS
- DN 70:94799
- TI Effects of Tween 80 and Freon 113 on measles virus
- AU Parisius, Wolf; Macmorine, Hilda G.
- CS Connaught Med. Res. Lab., Univ. Toronto, Willowdale, Ont., Can.
- SO Appl. Microbiol. (1969), 17(3), 379-83 CODEN: APMBAY
- DT Journal
- LA English
- AB Measles vaccines were prepd. from the same virus fluids by inactivation with HCHO or by extn. with ether, ethyl acetate, or Freon 113 in the presence of Tween 80. Tests of antigenic potency, based on antibody levels in guinea pigs, showed that the HCHO-inactivated vaccines were more potent than the solvent-inactivated prepns. and had the addnl. advantage of long shelf life. Residual Tween 80 in the solvent-extd. vaccines resulted in marked loss of immunogenic potency without significant loss of hemagglutinating activity. Neither extn. with organic solvents nor exhaustive dialysis efficiently removed Tween 80 from aq. solns.

=> d kwic 11

- L48 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- AB . . . potency without significant loss of hemagglutinating activity. Neither extn. with organic solvents nor exhaustive dialysis efficiently removed Tween 80 from aq. solns.
- IT Sorbitan, monooleate, polyoxyethylene derivs.
 RL: BAC (Biological activity or effector, except adverse); BIOL
 (Biological study)
 - (measles virus response to, vaccine antigenicity in relation

=> d bib abs hitstr 12

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ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2001 ACS
    1968:446063 HCAPLUS
AN
DN
     69:46063
ΤI
     Inactivation of myxoviruses
IN
    Kanarek, Alexander D.
PA
    Wellcome Foundation Ltd.
    Ger., 7 pp.
    CODEN: GWXXAW
    Patent
```

DT

LA German

FAN.	.CNT 1		
	PATENT NO.	KIND DATE	APPLICATION NO. DATE
ΡI	DE 1270223	19680612	
PRAI	I GB	19640320	
AB	Aq. suspensions	of myxoviruses,	(I), were inactivated with concu
	preservation of	antigenicity by	treating with 8-30 vol. % of chl
	Aq. suspensions preservation of	of myxoviruses, antigenicity by	(I), were inactivated with o

urrent lorinated or chlorinated and fluorinated hydrocarbons, at pH 6-8 in the presence of .gtoreq.0.05 wt. % of a nonionic wetting agent. Thus, a 6.25% by vol. aq. soln. of polyoxyethylene sorbitan monooleate (9 ml.) was added to the centrifuged culture liquor (441 ml.) of a measles virus grown on a chick embryo tissue culture and then intimately mixed with C12C:CC12 (50 ml.) at room temp. for 1 hr. solvent was centrifuged and the aq. phase retained as a primary vaccine. Also inactivated were influenza (A, B and C), Newcastle disease, rubella, parainfluenza and respiratory syncytial viruses with other hydrocarbons, e.g., CC14, C1CH:CC12, C12CFCF2C13, (C13C)2CH2 and Cl2C:CClCCl:CCl2, in the presence of, e.g., polyoxyethylene ethers of partial esters of lauric, palmitic or stearic acids. cf. U.S. 2,798,835 (CA 51: 15072i).

=> d kwic 12

L48 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2001 ACS . at pH 6-8 in the presence of .gtoreq.0.05 wt. % of a nonionic wetting agent. Thus, a 6.25% by vol. aq. soln. of polyoxyethylene sorbitan monooleate (9 ml.) was added to the centrifuged culture liquor (441 ml.) of a measles virus grown on a. . (50 ml.) at room temp. for 1 hr. The solvent was centrifuged and the aq. phase retained as a primary vaccine. Also inactivated were influenza (A, B and C), Newcastle disease, rubella, parainfluenza and respiratory syncytial viruses with other hydrocarbons, e.g., CCl4, ClCH:CCl2, Cl2CFCF2Cl3, (Cl3C)2CH2 and Cl2C:CClCCl:CCl2, in the presence of, e.g., polyoxyethylene ethers of partial esters of lauric, palmitic or stearic acids. cf. U.S. 2,798,835 (CA 51: 15072i).

=> d bib abs hitstr 13

ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2001 ACS L48

1960:70822 HCAPLUS AN

DN 54:70822

OREF 54:13564a-d

TI Mouthwashes

IN Bouchal, Alexander W.

PA Colgate-Palmolive Co.

DΤ Patent

LA Unavailable

FAN.CNT 1

PATENT NO. KIND APPLICATION NO. DATE

US 2921885 19600119

US A soln. of 0.3% (diisobutylcresoxyethoxyethyl)dimethylbenzylammonium chloride (I) and 0.2% Na N-lauroylsarcosine (II) is prepd. in distd. H2O. For example, standard disk-halo tests of this soln. against Micrococcus pyogenes, var. aureus (Staphylococcus aureus) showed that this compn. prevented baterial growth over an area 135% greater than that in which 0.03% of I alone was used. Doubling the amt. of I to 0.06% resulted in only a 15% increase in area of bacteriostasis over that of the 3% soln. Similarly, an aq. soln. contg. 0.03% I, 0.2% II, and 0.5% HO(C2H4O)a(C3H7O)b(C2H4O)cH (IV) in which the polypropylene oxide has a mol. wt. of 1500-800 and the polymerized ethylene oxide comprises 80-90% by wt. showed that this soln. prevented growth in an area 153% greater than that obtained with I alone. When 0.25% polyoxyethylene tridecyl alc. having about 12 ethylene oxide groups replaces the 0.5% IV in the above formula, the area of no bacterial growth is 300% more than that from the use of I alone. A soln. of I, 0.2% Na N-lauroyl-.beta.-alanine, and 0.5% IV in distd. H2O prevented bacterial growth in an area 52% greater than that obtained with I alone. A mouth rinse (a) was prepd. contg. I 0.03, II 0.2, IV 0.5, EtOH 15, adjuvants 0.2, and H2O 84.07%. Standard disk-halo tests against S. aureus and Lactobacillus K. gave a halo diam. of 23.5 mm. and 21.2 mm., resp. A mouth rinse (b) contained I 0.03, II 0.2, IV 0.5, EtOH 5, glycerol 0.1, adjuvants 0.1, and H2O 84.17%. A halo of 22.5 mm. was obtained against S. aureus and Lactobacillus. The mouth rinse (a) was tested in vivo by a panel of 12 persons and found to be more effective as compared with other mouth

=> d bib abs hitstr 1

L36 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS

1988:73342 HCAPLUS AN

108:73342 DN

ΤI Synergistic effect of detergents and aluminum phosphate on the humoral

immune response to bacterial and viral membrane proteins

AII Teerlink, Tom; Beuvery, E. Coen; Evenberg, Dolf; Van Wezel, Toon L.

CS Dep. Bact. Vaccines, Natl. Inst. Public Health Environ. Hyg. (RIVM),

Bilthoven, 3720 BA, Neth.

Vaccine (1987), 5(4), 307-14 CODEN: VACCDE; ISSN: 0264-410X so

חת Journal

LA English

The influence of detergents on the immunogenic activity of the major outer membrane protein of Neisseria gonorrhoeae was investigated. Most detergents tested enhanced the immune response. This effect was synergistic with the adjuvant activity of AlPO4. The combination of detergent and AlPO4 showed a stronger adjuvant activity than Freund's complete adjuvant. The adjuvant effect was only obsd. with protein prepns. with very low lipopolysaccharide content. The immunostimulating effect of detergents was also obsd. with meningococcal group C polysaccharide conjugated to a Haemophilus influenzae type b outer membrane protein and

with the fusion protein of measles virus. The influence of some detergent parameters (crit. micelle concn., hydrophile-lipophile balance,

and charge) was investigated.

9002-93-1, Triton X-100 9004-95-9, Brij 58 9004-99-3, Myrj 45 IT

RL: BIOL (Biological study)

(immune adjuvant activity of, aluminum phosphate synergism with, in response to bacterial and viral membrane proteins)

9002-93-1 HCAPLUS RN

CNPoly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ \text{Me} & & & \\ & & & \\ \text{Me} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

9004-95-9 HCAPLUS RN

CN Poly(oxy-1,2-ethanediyl), .alpha.-hexadecyl-.omega.-hydroxy- (9CI) (CA

HO
$$CH_2-CH_2-O$$
 CH_2 CH_2 CH_2 CH_2 CH_2 CH_2

9004-99-3 HCAPLUS RN

CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI) (CA INDEX NAME)

Me-
$$(CH_2)_{16}$$
 - C - CH_2 - CH

=> d bib abs hitstr 2 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS L36 1986:532044 HCAPLUS DN 105:132044 Immunogenic complex and its use as an immune stimulant, vaccines and ΤI reagent IN Morein, Bror Swed. Eur. Pat. Appl., 65 pp. CODEN: EPXXDW חת Patent LA English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE EP 180564 A2 19860507 EP 1985-850326 19851016 PТ EP 180564 А3 19880601 EP 180564 В1 19910717 R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE AT 65186 19910815 AT 1985-850326 Ε 19851016 CA 1275042 19901009 CA 1985-493583 19851022 Α1 FI 8504158 Α 19860502 FI 1985-4158 19851023 FI 86801 19920715 FI 86801 С 19921026 ZA 1985-8157 19851023 ZA 8508157 19860625 Α DK 8504985 Α 19860502 DK 1985-4985 19851030 DK 166653 В1 19930628 NO 8504355 19860502 NO 1985-4355 19851031 Α NO 167076 19910624 В NO 167076 C 19911002 JP 1985-245270 A2 JP 61129136 19860617 19851031 JP 07116056 В4 19951213 19861201 ES 1985-548412 ES 548412 A1 19851031 AU 8549383 A1 19860508 AU 1985-49383 19851106 AU 589915 В2 19891026 ZA 8607792 Α 19870527 ZA 1986-7792 19861014 CA 1275246 **A1** 19901016 CA 1986-520464 19861015 WO 8702250 Α1 19870423 WO 1986-SE480 19861016 W: AU, DK, FI, JP, NO, US RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE 19870505 AU 1986-64752 AU 8664752 Α1 19861016 AU 590904 В2 19891123 19871028 EP 242380 A1 EP 1986-906026 19861016 19910403 EP 242380 В1 R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE JP 63501078 19880421 JP 1986-505483 т2 19861016 JP 07051514 В4 19950605 19880816 ES 2002532 Α6 ES 1986-2624 19861016 AT 62135 19910415 AT 1986-906026 19861016 Е US 5254339 19931019 US 1987-70920 19870601 Α FI 8702647 19870615 FI 1987-2647 19870615 FI 86597 В 19920615 19920925 FI 86597 С NO 8702484 Α 19870615 NO 1987-2484 19870615 19911230 NO 168806 В NO 168806 С 19920408 DK 8703029 19870814 DK 1987-3029 19870615 DK 165360 19921116 19930405 DK 165360 PRAI SE 1984-5493 19841101 EP 1985-850326 19851016 EP 1986-906026 19861016 WO 1986-SE480 19861016 19870601 WO 1987-SE480 An immunogenic complex is prepd. by (1) mixing antigenic biol. material with a solubilizing agent to form a complex between the solubilizing agent and proteins or peptides in the material; (2) transferring the proteins or peptides from the complex with solubilizing

agent to a soln. of a glycoside with which they formed a complex serving as a carrier mol.; (3) coupling .gtoreq. 1 antigens or haptens to the carrier. For example, envelope proteins from influenza virus strain PR8 were solubilized with 20% N-decanoyl-N-methylglucamine and sepd. from the core structure by centrifugation through 20% sucrose contg. the detergent at a concn. > than the crit. micellar concn. The collected proteins, with 0.1% Quil A (saponin) added to form a complex, were dialyzed against 0.9% NaCl and coupled to LH-RH with glutaraldehyde. Mice immunized with this LH-RH conjugate showed a strong immune response with no side effects.

IT 9002-93-1

RL: BIOL (Biological study)

(as solubilizer, in antigen carrier prepn.)

RN 9002-93-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me} & \text{Me} \end{array}$$

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=> d bib abs hitstr 3
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 $HO - CH_2 - CH_2 - O - CH_2 - CH_2$

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ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS
     1985:600769 HCAPLUS
AN
     103:200769
DN
ΤI
     Contribution to the investigation of micellar solubilization -
     specific case of surfactant mixtures
     Vaution, Catherine; Treiner, Claude
     Fac. Pharm., Univ. Paris-Sud, Chatenay-Malabry, 92290, Fr.
CS
     S.T.P. Pharma (1985), (4), 333-40
     CODEN: STPPEF
DT
     Journal
LA
     French
     \begin{tabular}{ll} \textbf{Micellar} & solubilization is generally characterized by soly. \end{tabular}
AB
     coeff. or partition coeff. The soly. coeff (k) is given by Ct /Caq = 1 + kCs; where Ct = total concn. of the solute present in
     the micellar soln., Caq = concn. of the solute dissolved in
     water, and Cs = concn. of adjuvant (in the case of
     micellar solubilization, the adjuvant is a surfactant).
     The value of partition coeff. K (also described by various math. equations) is characteristic of the surfactant used for a given temp. and
     pressure. The value is const. under conditions in which the solute
     behaves as an ideal compd. in the 2 phases (a micellar soln.
     consists of an aq. phase and inseparable micellar phase or
     pseudo-phase). During micellar solubilization, the solute is
     always weakly sol. in the aq. phase. This implies that the solute-solute
     interaction can be considered as 0 and the activity coeff. (f) = 1. On
     the contrary, the solute is bound in the micelles at relatively
     elevated concns. In this case relatively strong interactions can occur in
     the micellar phase. The pseudo-phase model was validated by
     detg. the logarithm of partition coeff. in a micellar system as
     a function of logarithm of partition coeff. in a biphasic system.
     Trimethyldodecylammonium bromide [1119-94-4] (cationic surfactant) and Na
     dodecyl sulfate [151-21-3] (anionic surfactant) were used as the model
     compds. Micellar solubilization was also demonstrated in mixed
     micelle systems. The solubilizing capacity and the partition
     coeff. were detd. as a function of effective compn. of mixed
     micelles.
     9002-92-0
     RL: PROC (Process)
         (micellar solubilization of)
     9002-92-0 HCAPLUS
     Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI)
CN
     INDEX NAME)
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ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS
     1998:629681 HCAPLUS
AN
     130:57111
DN
     Synthesis, physicochemical properties and immunoadjuvant activity of
TΙ
     water-soluble phosphazene polyacids
     Andrianov, Alexander K.; Sargent, Jonathan R.; Sule, Sameer S.; Le Golvan,
     Mark P.; Woods, Angela L.; Jenkins, Sharon A.; Payne, Lendon G.
     Virus Research Institute, Inc., Cambridge, MA, 02138, USA
J. Bioact. Compat. Polym. (1998), 13(4), 243-256
CS
SO
     CODEN: JBCPEV; ISSN: 0883-9115
PB
     Technomic Publishing Co., Inc.
DT
     Journal
LA
     English
     Mixed-substituted polyphosphazenes contg. carboxylic acid and alkyl ether
     side groups were synthesized and characterized. Physicochem. properties
     of phosphazene polyacids in aq. solns. were
     investigated as a function of copolymer structure and compn. The
     immunoadjuvant activity of polyphosphazenes was evaluated by studying the
     effect of copolymers on the immunogenicity of the influenza virus
     in mice. The polyphosphazenes demonstrated the ability to enhance the
     immune response as compared to the levels elicited by the vaccine
     alone.
     109-86-4DP, 2-Methoxyethanol, reaction products with
     polyphosphazene, hydrolyzed 111-77-3DP, 2-(2-
     Methoxyethoxy)ethanol, reaction products with polyphosphazene, hydrolyzed
     9004-74-4DP, Polyethylene glycol methyl ether, reaction products
     with polyphosphazene, hydrolyzed
     RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL
      (Biological study); PREP (Preparation); USES (Uses)
         (prepn. and physicochem. properties and immunoadjuvant activity of
         water-sol. phosphazene polyacids)
     109-86-4 HCAPLUS
RN
     Ethanol, 2-methoxy- (8CI, 9CI) (CA INDEX NAME)
CN
но-сн2-сн2-о-сн3
     111-77-3 HCAPLUS
RN
     Ethanol, 2-(2-methoxyethoxy)- (6CI, 8CI, 9CI) (CA INDEX NAME)
CN
{\tt MeO-CH_2-CH_2-O-CH_2-CH_2-OH}
     9004-74-4 HCAPLUS
     Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxy- (9CI) (CA INDEX
CN
     СН2-СН2-О-СН3
RE.CNT 13
(1) Allcock, H; Biodegradable Polymers as Drug Delivery Systems 1990, P163
(2) Allcock, H; Biomaterials 1996, V17, P2295 HCAPLUS
(3) Allcock, H; Macromolecules 1986, V19, P1508 HCAPLUS
(4) Allcock, H; Macromolecules 1989, V22, P75 HCAPLUS
(5) Allcock, H; Macromolecules 1996, V29, P1313 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
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- ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS
- 1998:127592 HCAPLUS AN
- DN 128:261743
- ТI Elutability of proteins from aluminum-containing vaccine adjuvants by treatment with surfactants
- Rinella, Joseph V., Jr.; Workman, Ryan F.; Hermodson, Mark A.; White, Joe L.; Hem, Stanley L.
- Dep. Industrial and Physical Pharmacy, Chemistry, Biochemistry, and CS Agronomy, Purdue Univ., West Lafayette, IN, 47907, USA
- J. Colloid Interface Sci. (1998), 197(1), 48-56 so CODEN: JCISA5; ISSN: 0021-9797
- Academic Press PΒ
- DT Journal
- LA
- English The elutability of proteins from adjuvants in model vaccines composed of ovalbumin adsorbed by aluminum hydroxide adjuvant or lysozyme adsorbed by aluminum phosphate adjuvant following treatment with surfactant solns. was studied. Nonionic (Triton X-100, lauryl maltoside), zwitterionic (lauryl sulfobetaine), anionic (sodium dodecyl sulfate), and cationic (cetylpyridinium chloride, dodecyltrimethylammonium chloride) surfactants were investigated. Cetylpyridinium chloride produced the greatest degree of elution (60%) of ovalbumin from aluminum hydroxide adjuvant. Sodium dodecyl sulfate completely eluted lysozyme from aluminum phosphate adjuvant. The effectiveness of surfactants in removing preadsorbed proteins was directly related to their ability to denature the protein. Micellar solubilization and electrostatic repulsion may also contribute to desorption.
- TΤ **9002-93-1**, Triton X-100 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (elutability of proteins from aluminum-contg. vaccine adjuvants by treatment with surfactants)
- RN 9002-93-1 HCAPLUS
- Poly(oxy-1,2-ethanediy1), .alpha.-[4-(1,1,3,3-tetramethylbuty1)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

- ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS L39
- 1988:636812 HCAPLUS AN
- 109:236812 DN
- Controlled organization of multimolecular complexes of enveloped ΤI virus glycoproteins: study of immunogenicity
- ΑU Berezin, V. E.; Zaides, V. M.; Isaeva, E. S.; Artamonov, A. F.; Zhdanov, V. M.
- D. I. Ivanovskii Inst. Virol., Moscow, 123098, USSR Vaccine (1988), 6(5), 450-6 CS
- SO CODEN: VACCDE; ISSN: 0264-410X
- \mathbf{DT} Journal
- LA English
- Some technol. and immunol. problems facing the prepn. of subunit viral vaccines are discussed. Solubilization of enveloped virus glycoproteins with various detergents was studied. A novel non-ionic detergent, MESK, can be used to prep. the glycoproteins of enveloped viruses in defined supramol. forms: monomers, micelles, liposomes, and multimeric complexes. These prepns. were tested for immunogenicity. The immunogenicity of glycoproteins in micellar form or in liposomes is comparable with that of the whole virus. The immunogenicity of the glycoprotein complex with the glycoside Quil A appeared to be significantly higher in comparison with the whole virus and was similar to the immunogenicity of glycoproteins mixed with Freund's complete adjuvant.
- 9002-93-1, Triton X-100
 - RL: BIOL (Biological study)
 - (in enveloped virus glycoprotein supramol. forms prepn., vaccine in relation to)
- RN9002-93-1 HCAPLUS
- Poly(oxy-1, 2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me} & \text{Me} \end{array}$$

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=> d bib abs hitstr 1
     ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2001 ACS
     1998:208885
                  HCAPLUS
AN
     128:190536
DN
     Enhancement of the Diffusion of Active Ingredients in Barley Leaf
ΤT
     Cuticular Wax by Monodisperse Alcohol Ethoxylates
     Burghardt, Markus; Schreiber, Lukas; Riederer, Markus
     Lehrstuhl fuer Botanik IIOekophysiologie und Vegetationsoekologie
     Biozentrum, Universitaet Wuerzburg, Wuerzburg, D-97082, Germany
     J. Agric. Food Chem. (1998), 46(4), 1593-1602
CODEN: JAFCAU; ISSN: 0021-8561
SO
PΒ
     American Chemical Society
DT
     Journal
LA
     English
     Rates of uptake of active ingredients (ai) across the plant cuticle are
     enhanced by the action of alc. ethoxylate (AE) adjuvants.
     partitioning of monodisperse AE between ag. solns. and
     isolated cuticular wax from barley (Hordeum vulgare L.) leaves was
     investigated.
                    Quant. structure-property relationships for wax/water
     partition coeffs. (Kwax/w) and max. AE concns. in the wax (cwaxmax) were
     established. In the presence of AE, the diffusion coeffs. of six ai in
     cuticular wax increased by factors of up to 125. AE effects were linearly
     related to their resp. cwaxmax, suggesting a common intrinsic activity.
     AE had higher effects on the diffusion coeffs. of large ai than on those
     of smaller ones. Conclusions are drawn concerning the mechanism of AE
     action on the phys. structure of cuticular waxes.
     112-34-5, Diethylene glycol monobutyl ether 3055-93-4,
     Diethylene glycol monododecyl ether 3055-94-5, Triethylene glycol monododecyl ether 3055-95-6, Pentaethylene glycol
     monododecyl ether 3055-96-7, Hexaethylene glycol monododecyl
     ether 3055-97-8, Heptaethylene glycol monododecyl ether
     3055-98-9, Octaethylene glycol monododecyl ether 5274-68-0
       Tetraethylene glycol monododecyl ether 5698-39-5, Octaethylene
     glycol monohexadecyl ether 19327-39-0, Tetraethylene glycol
     monooctyl ether 23244-49-7, Pentaethylene glycol monodecyl ether
     24233-81-6, Octaethylene glycol monodecyl ether 25961-89-1
       Triethylene glycol monohexyl ether 27847-86-5, Octaethylene
     glycol monotetradecyl ether 40036-79-1, Heptaethylene glycol
     monotetradecyl ether
     RL: AGR (Agricultural use); BAC (Biological activity or effector, except
     adverse); PRP (Properties); BIOL (Biological study); USES (Uses)
        (enhancement of the diffusion of active ingredients in barley leaf
        cuticular wax by monodisperse alc. ethoxylates)
RN
     112-34-5 HCAPLUS
CN
     Ethanol, 2-(2-butoxyethoxy)- (8CI, 9CI) (CA INDEX NAME)
n-BuO-CH_2-CH_2-O-CH_2-CH_2-OH
     3055-93-4 HCAPLUS
     Ethanol, 2-[2-(dodecyloxy)ethoxy]- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
CN
{\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me}
RN
     3055-94-5 HCAPLUS
     Ethanol, 2-[2-[2-(dodecyloxy)ethoxy]ethoxy]- (6CI, 7CI, 8CI, 9CI) (CA
CN
     INDEX NAME)
{\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me}
RN
     3055-95-6 HCAPLUS
     3,6,9,12,15-Pentaoxaheptacosan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
```

PAGE 1-A
HO-CH₂-CH₂-CH₂-CH₂-O-CH₂

PAGE 1-B

- (CH₂)₁₁-Me

RN 3055-96-7 HCAPLUS CN 3,6,9,12,15,18-Hexaoxatriacontan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

 $\label{eq:page_1-A} \mbox{HO-CH}_2-\mbox{CH}_2-\mbox{CH}_2-\mbox{O-CH}_2-\mbox{CH}_2-\mb$

· PAGE 1-B

-- CH₂-- CH₂-- O-- (CH₂)₁₁-- Me

RN 3055-97-8 HCAPLUS CN 3,6,9,12,15,18,21-Heptaoxatritriacontan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

PAGE 1-A
HO-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂

PAGE 1-B

 $-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me$

RN 3055-98-9 HCAPLUS CN 3,6,9,12,15,18,21,24-Octaoxahexatriacontan-1-ol (7CI, 8CI, 9CI) (CA INDEX NAME)

 $\label{eq:page_1-a} \mbox{PAGE } 1\mbox{-A} \\ \mbox{HO-CH}_2\mbox{-CH}_2\mbox{-O-CH}_2\mbox{-CH}_2\mbox{-O-CH}_2\mbox{-CH}_2\mbox{-O-CH}_2\mbox{-CH}_2\mbox{-O-CH}_2\mbox{-CH}_2\mbox{-O-CH}_2\mbo$

PAGE 1-B

 $-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me$

RN 5274-68-0 HCAPLUS CN 3,6,9,12-Tetraoxatetracosan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

 ${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me}$

RN 5698-39-5 HCAPLUS CN 3,6,9,12,15,18,21,24-Octaoxatetracontan-1-ol (7CI, 8CI, 9CI) (CA INDEX NAME)

PAGE 1-A HO-CH₂-CH₂-CH₂-O-CH₂-CH₂-CH₂-O-CH₂-CH₂-CH₂-CH₂-O-CH₂-

PAGE 1-B

 $-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{15}-Me$

RN 19327-39-0 HCAPLUS CN 3,6,9,12-Tetraoxaeicosan-1-ol (6CI, 8CI, 9CI) (CA INDEX NAME)

 $HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)$ 7 - Me

RN 23244-49-7 HCAPLUS CN 3,6,9,12,15-Pentaoxapentacosan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

 $\label{eq:page 1-A} \mbox{ PAGE 1-A } \\ \mbox{ HO-CH$_2$-CH$_2$-O-CH$_2$-CH$_2$-O-CH$_2$-CH$_2$-O-CH$_2$-CH$_2$-O-CH$

PAGE 1-B

- (CH₂)₉-Me

RN 24233-81-6 HCAPLUS CN 3,6,9,12,15,18,21,24-Octaoxatetratriacontan-1-ol (8CI, 9CI) (CA INDEX NAME)

PAGE 1-A
HO-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂-CH₂-O-CH₂

PAGE 1-B

 $-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_9-Me$

RN 25961-89-1 HCAPLUS CN Ethanol, 2-[2-[2-(hexyloxy)ethoxy]- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

 ${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_5-Me}$

RN 27847-86-5 HCAPLUS
CN 3,6,9,12,15,18,21,24-Octaoxaoctatriacontan-1-ol (8CI, 9CI) (CA INDEX NAME)

 $\label{eq:page_1-a} \mbox{ PAGE 1-A} \\ \mbox{ HO-CH}_2-\mbox{CH}_2-\mbox{CH}_2-\mbox{O-CH}_2-\mbox{CH}$

PAGE 1-B

 $-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{(CH}_2)_{13}-\text{Me}$

RN 40036-79-1 HCAPLUS CN 3,6,9,12,15,18,21-Heptaoxapentatriacontan-1-ol (6CI, 9CI) (CA INDEX NAME)

PAGE 1-A

 ${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-$

PAGE 1-B

 $-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{13}-Me$

=> d bib abs hitstr 2

L40 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2001 ACS

1994:71539 HCAPLUS ΑN

120:71539 DN

ΤI Physical properties of silicone surfactants for agrochemical applications Murphy, Dennis S.; Policello, George A.; Goddard, Errol D.; Stevens, Peter J. G.

CS

Union Carbide Corp., Tarrytown, NY, 10591, USA
ASTM Spec. Tech. Publ. (1993), 1146(Pesticide Formulations and
Applications Systems, 12th Vol.), 45-56 SO CODEN: ASTTA8; ISSN: 0066-0558

DT Journal

LA English

AΒ Aq. solns. of four silicone surfactants, and two hydrocarbon surfactants were studied over a range of concns. for dynamic surface tension lowering, spreading on paraffin wax film, and static surface tension. Dynamic surface tension profiles were obtained by both the oscillating jet method and the max. bubble pressure method. It was found that \mathbf{aq} . \mathbf{solns} . of the silicone surfactants lower surface tension more quickly, spread better on paraffin wax film, and yielded lower static surface tension values than corresponding aq. solns. of the hydrocarbon surfactants. Implications of the findings as regards effectiveness of these adjuvants are discussed.

ΙT 2315-64-2

RL: PRP (Properties) (phys. properties of, silicone surfactants for agrochem. applications in relation to)

RN 2315-64-2 HCAPLUS

CN (9CI) (CA INDEX NAME)

PAGE 1-A

HO-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O

PAGE 1-B

V

=> d bib abs hitstr 3

- L40 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- AN 1991:519977 HCAPLUS
- DN 115:119977
- TI Enhancing properties of surfactants on the release of carbamazepine from suppositories
- AU Fontan, J. E.; Arnaud, P.; Chaumeil, J. C.
- CS Dep. Pharmacotech., Fac. Sci. Pharm. Biol., Paris, 75270, Fr.
- SO Int. J. Pharm. (1991), 73(1), 17-21 CODEN: IJPHDE; ISSN: 0378-5173
- DT Journal
- LA English
- The effect of surfactants on physicochem. properties and on the release characteristics of carbamazepine from fatty suppositories was investigated in vitro. Four surfactants, polyoxyethylene 50-stearate (Simulsol M), polyoxyethylene 23-lauryl ether (Brij 35), and polysorbates 20 and 80, were examd. as adjuvants. The dissoln. rate was enhanced by all surfactants used. The dissoln. rate at 30 min increased from 54% without surfactant, to 100% with polysorbate 80 (2%). The liquefaction time could be the limiting factor for the dissoln. rate of carbamazepine. The better solubilizing effect of polysorbate 80 can be due to the better incorporation capacity of its micelle.
- IT 9002-92-0, Brij 35 9004-99-3, Simulsol M RL: BIOL (Biological study)
 - (carbamazepine release from suppositories enhancement by)
- RN 9002-92-0 HCAPLUS

$$HO = \begin{bmatrix} -CH_2 - CH_2 - O \end{bmatrix}_n (CH_2)_{11} - Me$$

- RN 9004-99-3 HCAPLUS
- CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI) (CA INDEX NAME)

om above

- L40 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- AN 1990:434374 HCAPLUS
- DN 113:34374
- TI Solubilization of unconjugated bilirubin and its calcium salts by ionic, amphoteric, and nonionic detergents
- AU Wosiewitz, U.; Leuschner, U.
- CS Abt. Gastroenterol., Universitaetsklin., Zent. Inneren Med., Frankfurt, D-6000, Fed. Rep. Ger.
- SO Naturwissenschaften (1990), 77(5), 232-4 CODEN: NATWAY; ISSN: 0028-1042
- DT Journal
- LA English
- AB Bile salts (BS) have been used as adjuvants in local chemolysis of pigment gallstones (PS), because these anionic detergents were found to solubilize unconjugated bilirubin (UCB), an obligatory product of PS chemolysis, and even its calcium salts, the main constituents of human PS. Since local chemolitholysis takes too much time in many cases, current irrigation media have to be improved. One of the possible approaches could be the substitution of the BS by another detergent with a higher solubilization efficiency for UCB and calcium bilirubinate. The soly. of UCB crystals as well as of amorphous CaB/Ca(BH)2 depended on the surrounding pH and on the kind of detergent used. The highest (apparent) solubilities of UCB were found with nonionic (but polar), the lowest with anionic detergents, namely, with SDS. The considerable net (neg.) charge of the latter (more than 60 mols. per micelle) perhaps gives rise to repulsive forces which cause a decrease in soly. From the effects of the cationic hexadecyltrimethylammonium bromide it seems very likely that the elec. net charges of the detergents, which for their part are influenced by the pH, play an important role in the solubilization of UCB and its Ca salts. The results obtained in vitro suggest that improvement of local chemolysis of pigment material is possible in vivo, if nontoxic detergents are available with a greater solubilization efficacy than BS.
- IT 9002-92-0 RL: BIOL (Biological study)
 - (gallstone pigment materials solubilization by, elec. charge in relation to)
- RN 9002-92-0 HCAPLUS

HO
$$-CH_2-CH_2-O$$
 (CH₂)₁₁-Me

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=> d bib abs hitstr 5
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```
L40
    ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2001 ACS
```

1989:548771 HCAPLUS AN

111:148771 DN

ΤI Foliar absorption of some nonionic surfactants from aqueous solutions in the absence and presence of pesticidal active ingredients

Silcox, Dawn; Holloway, Peter J. ΑU

CS

Agric. Prod. Res. Dev., Dow Chem., Wantage, UK Adjuvants Agrochem. (1989), Volume 1, 115-28. Editor(s): Chow, Paul N. P. SO. Publisher: CRC, Boca Raton, Fla. CODEN: 560MA9

DT Conference

LA English

Foliar uptake expts. with 14C-labeled linear alcs. (C12E8, C13E6, C18E8.5) AB and alkylphenol poloxyethylene surfactants (OPE7, OPE9.5, NPE5.5, NPE9.5) demonstrated that considerable quantities of such compds. can enter plants following droplet applications of dil. aq. solns. The rates and total amts. of uptake varied greatly according to plant species, and both were influenced by the chem. nature of the surfactant. The surfactants examd. had hydrophile-lipophile balance (HLB) values in the range 10 to 14, and max. foliar absorption was obsd. for compds. having a C12/C13 alkyl chain as the hydrophobic moiety. There was little movement of any of the surfactants following penetration into leaves, but they were subsequently metabolized within the treated areas, the rate and products of metab. again differing with plant species. On Vicia faba leaves, surfactant uptake was altered greatly in the presence of a no. of different water-sol. agrochems., anionic compds. slowing absorption to a greater extent than cationic ones. The intimate relationship between surfactant and chem. during foliar penetration was confirmed by further expts. on the same plant with the 14C-labeled herbicide difenzoquat. The implications of the findings in terms of elucidating the possible mode of action of surfactants as spray adjuvants are discussed.

930-09-6, 3,6,9,12,15,18-Hexaoxahentriacontan-1-ol

3055-98-9 9002-93-1 9005-00-9

26027-38-3

RL: PROC (Process)

(foliar absorption of, in presence or absence of pesticides)

930-09-6 HCAPLUS RN

3,6,9,12,15,18-Hexaoxahentriacontan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX CN NAME)

PAGE 1-A

HO-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-

PAGE 1-B

- CH $_2-$ CH $_2-$ O- (CH $_2$) $_{12}-$ Me

3055-98-9 HCAPLUS RN

3,6,9,12,15,18,21,24-Octaoxahexatriacontan-1-ol (7CI, 8CI, 9CI) (CA INDEX

PAGE 1-A

HO-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2

PAGE 1-B

 $- \, \mathrm{CH}_2 - \, \mathrm{CH}_2 - \, \mathrm{O} - \, \mathrm{CH}_2 - \, \mathrm{CH}_2 - \, \mathrm{O} - \, \mathrm{CH}_2 - \, \mathrm{CH}_2 - \, \mathrm{O} - \, \, (\mathrm{CH}_2) \, \mathbf{11} - \mathrm{Me}$

RN

9002-93-1 HCAPLUS
Poly(oxy-1,2-ethanediy1), .alpha.-[4-(1,1,3,3-tetramethylbuty1)pheny1]-.omega.-hydroxy- (9CI) (CA INDEX NAME) CN

$$\begin{array}{c|c} \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me} & \text{OH}_2\text{-CH}_2 \\ \text{Me} & \text{Me} \end{array}$$

RN

9005-00-9 HCAPLUS Poly(oxy-1,2-ethanediyl), .alpha.-octadecyl-.omega.-hydroxy- (9CI) (CA CNINDEX NAME)

$$HO - CH_2 - CH_2 - O - CH_2 - CH_2 - O - C$$

RN 26027-38-3 HCAPLUS

Poly(oxy-1,2-ethanediyl), .alpha.-(4-nonylphenyl)-.omega.-hydroxy- (9CI) CN (CA INDEX NAME)

$$O-CH_2-CH_2$$
 OH

Me- (CH₂) 8

- ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2001 ACS L40
- 1987:483791 HCAPLUS
- DN 107:83791
- Effects of sodium taurodihydrofusidate on nasal absorption of insulin in ΤI sheep
- ΑU Longenecker, John P.; Moses, Alan C.; Flier, Jeffrey S.; Silver, Robert D.; Carey, Martin C.; Dubovi, Edward J.
 California Biotechnol., Inc., Mt. View, CA, 94134, USA
 J. Pharm. Sci. (1987), 76(5), 351-5
- CS
- SO CODEN: JPMSAE; ISSN: 0022-3549
- DT Journal
- LA English
- To investigate the utility of a novel adjuvant, Na taurodihydrofusidate (STDHF), as an enhancer of mucosal permeation of drugs, expts. involving intransel insulin-STDHF administration in sheep were performed. Rabbit erythrocyte lysis assays were employed to assess the relative membrane lytic activity of STDHF, as well as that of its glycine-conjugated analog, compared with a nonionic detergent and a common bile salt. Equiv. wt. concns. of the fusidates were 5- to 10-fold less lytic than the bile salt and at least 100-fold less lytic than the nonionic detergent laureth-9. Provided the concn. of STDHF was greater than its crit. micellar concn., formulations of insulin with STDHF greatly enhanced intranasal insulin absorption. Optimal nasal insulin absorption was attained at a molar ratio of STDHF to insulin of 5:1. In addn., intranasal absorption was linearly related to insulin dose. Compared with i.v. administration, the mean bioavailability of intranasal insulin was 16.4%. Interovine variability was low, with a coeff. of variation of 14% for 12 animals. Intranasal absorption of Na insulin was not significantly different from that of Zn insulin. However, formulations of both cryst. insulin prepns. were absorbed more efficiently than a formulation prepd. using com. available solns. of U-500 insulin. The results taken together indicate that STDHF is an excellent enhancer of insulin absorption from the nasal mucosa.
- 9002-92-0, Laureth 9
 - RL: BIOL (Biological study)
 - (insulin intranasal absorption enhancement by taurodihydrofusidate in relation to)
- RN 9002-92-0 HCAPLUS
- Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA CN

```
=> d bib abs hitstr 7
L40 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2001 ACS
     1986:193210 HCAPLUS
AN
ĎΝ
     104:193210
ΤI
     Erodible matrix for sustained release bioactive composition
     Snipes, Wallace C.
IN
    Zetachron, Inc., USA PCT Int. Appl., 31 pp.
PA
SO
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 2
     PATENT NO.
                      KIND DATE
                                            APPLICATION NO.
                                                             DATE
     WO 8600802
                            19860213
                                            WO 1985-US1349
                                                             19850717
PΙ
                       Al
         W: AU, JP, KP
         RW: BE, CH, DE, FR, GB, NL
     CA 1246448
                      A1 19881213
                                            CA 1985-486711
                                                             19850712
                            19860225
                                            AU 1985-46388
     AU 8546388
                       A1
                                                             19850717
     AU 573149
                       В2
                            19880526
    EP 190255
                       Α1
                            19860813
                                            EP 1985-903908
                                                             19850717
     EP 190255
                       В1
                            19921111
         R: BE, CH, DE, FR, GB, LI, NL
                       т2
                                            JP 1985-503436
     JP 61502759
                            19861127
                                                             19850717
PRAI US 1984-633604
                            19840723
     WO 1985-US1349
                            19850717
    A sustained-release oral compn. erodable in aq. soln.
     comprises 5-95% by wt. of PEG (mol. wt. 1000-20,000) and 95-5\% of an
     erosion rate modifier (e.g., fatty acid) which is amphiphilic and insol.
     in the aq. soln. Thus, compns. contg. PEGs 1000,
     4000, 8000, or 20,000 (37.5% each), myristic acid 15%, starch (22.5%), and
     indomethacin 25% all released the drug gradually over a period of several
TT
     9004-99-3
     RL: BIOL (Biological study)
        (sustained-release erodable matrix pharmaceutical compns. manuf. with)
RN
     9004-99-3 HCAPLUS
     Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI)
CN
     (CA INDEX NAME)
```

=> d bib abs hitstr 8

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ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2001 ACS
L40
      1984:169856 HCAPLUS
ΑN
DN
      100:169856
      Surface tension and contact angle of herbicide solutions affected by
ΤI
      surfactants
      Singh, Megh; Orsenigo, J. R.; Shah, D. O.
     Inst. Food Agric. Sci., Univ. Florida, Lake Alfred, FL, 33850, USA JAOCS, J. Am. Oil Chem. Soc. (1984), 61(3), 596-600 CODEN: JJASDH
CS
DT
      Journal
LA
      English
```

GΙ

Contact angle and surface tension were measured for distd. H2O and hard water solns. of adjuvants Ortho X-77 [12687-90-0], Span-20 [1338-39-2], Sterox-NJ [59644-67-6], Surfactant-WK [60828-78-6], Triton B-1956, Triton X-114 [9036-19-5], Tween-20 [9005-64-5], and Sun Oil 11E. The same parameters were measured for suspensions of atrazine (I) [1912-24-9] and ametryn [834-12-8] with and without each adjuvant. All adjuvants reduced surface tension and contact angle of H2O; surfactant-WK was most effective and Tween-20 was least effective. Increasing concn. of surfactants from 0 to 0.1% (vol./vol.) gave progressive redn. in surface tension and contact angle, whereas higher concns., 0.1-2.0% (vol./vol.), had no further effect. Surfactant-WK at 0.1% in H2O reduced surface tension from 72.8 to 27 dynes/cm and contact angle from 110.degree. to 41.degree.. An addnl. increase in Surfactant-WK concn. from 0.1 to 2% did not further reduce surface tension and contact angle. Sun Oil 11E was identical in behavior except that it was less effective than the surfactants. Water hardness .ltoreq.1000 ppm as Ca2+ did not affect surface tension and contact angle in surfactant solns. An aq. soln. of I had a higher surface tension and contact angle than ametryn in the absence of surfactants. However, these differences were not obsd. when surfactants were added to either herbicide.

IT 60828-78-6

RL: BIOL (Biological study) (contact angle and surface tension of herbicide solns. contq.)

60828-78-6 HCAPLUS RN

Poly(oxy-1,2-ethanediyl), .alpha.-[3,5-dimethyl-1-(2-methylpropyl)hexyl]-CN .omega.-hydroxy- (9CI) (CA INDEX NAME)

```
=> d bib abs hitstr 9
```

- ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2001 ACS L40
- AN 1983:95551 HCAPLUS
- DN 98:95551
- Vaginal absorption of a potent luteinizing hormone-releasing hormone ΤI analog (leuprolide) in rats. I: Absorption by various routes and absorption enhancement
- Okada, Hiroaki; Yamazaki, Iwao; Ogawa, Yasuaki; Hirai, Shinichiro; Yashiki, Takatsuka; Mima, Hiroyuki ΑU
- Cent. Res. Div., Takeda Chem. Ind., Ltd., Yodogawa, 532, Japan CS
- J. Pharm. Sci. (1982), 71(12), 1367-71 CODEN: JPMSAE; ISSN: 0022-3549 SO
- DТ Journal
- LA English
- The absorption of leuprolide [53714-56-0]by different routes was AB evaluated by detg. the ovulation-inducing activity in diestrous rats. Vaginal administration showed the greatest potency among nonparenteral routes and was followed successively by rectal, nasal, and oral administration. A mixed micellar soln. with monoolein [25496-72-4]-bile acids improved the intestinal absorption of leuprolide, and nasal absorption was enhanced by adding Na glycocholate [863-57-0], surfactin [24730-31-2], or polyoxyethylene 9 lauryl ether [9002-92-0], but these bioavailabilities were still insufficient. The vaginal absorption was enhanced by citric acid [77-92-9], succinic acid [110-15-6], tartaric acid [87-69-4], and glycocholic acid [475-31-0]; the abs. bioavailability increased to .apprx.20%. The vaginal absorption from jellies, as practical dosage forms, yielded sufficient activity of leuprolide, but absorption was slightly reduced with highly polar polymers or with higher concns. of polymers. Vaginal administration of leuprolide can be a rational dosage method for long-term antitumor therapy.
- TΤ 9002-92-0
 - RL: BIOL (Biological study)
- (leuprolide absorption by nose and vagina increase by)
- 9002-92-0 HCAPLUS RN
- Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) CN INDEX NAME)

HO
$$CH_2 - CH_2 - O - \frac{1}{n}$$
 (CH₂)₁₁ - Me

=> d bib abs hitstr 10

- L40 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- 1973:47733 HCAPLUS AN
- DN 78:47733
- TI Influence of auxiliary material on pharmaceuticals. 21. Mechanism of interaction between esters of nicotinic acid and poly(oxyethylene) ethers
- ΑU
- Ullmann, E.; Thoma, K.; Lippold, B. C. Inst. Pharm. Lebensmittelchem., Univ. Muenchen, Munich, Ger. CS
- SO Arch. Pharm. (Weinheim, Ger.) (1972), 305(11), 797-802
 - CODEN: ARPMAS
- DT Journal
- German LA
- AB The interactions between surface-active poly(oxyethylene) ethers and esters of nicotinic acid take place in the hydrophobic interior and in the hydrophilic exterior of the micelles. The degree of binding of the esters to the micelles depends particularly on the physicochem. properties of the esters. The lipophilic hexyl ester, e.g., is bound to a much greater extent than the hydrophilic Et ester. The structure of the surface-active agents has only a small effect. From the exptl. results, conclusions are drawn about the localization of the esters in the micelles.
- IT 9002-92-0 9004-95-9 9005-00-9

27306-79-2

RL: BIOL (Biological study)

(pharmaceutical adjuvants, nicotinates reaction with)

- 9002-92-0 HCAPLUS RN
- Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) CN INDEX NAME)

$$HO = \begin{bmatrix} CH_2 - CH_2 - O \end{bmatrix}_n (CH_2)_{11} - Me$$

- 9004-95-9 HCAPLUS RN
- CN Poly(oxy-1,2-ethanediy1), .alpha.-hexadecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)

- RN 9005-00-9 HCAPLUS
- CN Poly(oxy-1,2-ethanediyl), .alpha.-octadecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$HO \longrightarrow CH_2 - CH_2 - O \longrightarrow n$$
 (CH₂)₁₇ - Me

- 27306-79-2 HCAPLUS
- CN Poly(oxy-1,2-ethanediyl), .alpha.-tetradecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)

=> d bib abs hitstr 11

- L40 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2001 ACS 1968:509780 HCAPLUS AN DN 69:109780 Effect of adjuvants in the preparation of pharmaceuticals. XIX. ΤI Effect of surfactants on ester hydrolysis Ullmann, Elsa; Thoma, K.; Rombach, R. Inst. Pharm. Lebensmittelchem., Univ. Muenchen, Munich, Ger. CS Arch. Pharm. (Weinheim) (1968), 301(5), 363-9 CODEN: APBDAJ SO DТ Journal The stabilization of phenyl salicylate (I) by surfactants was detd. I hydrolyzed completely in aq. soln. at pH 7 and 20.degree. in 30 days. It was stabilized completely by 0.5% Na lauryl sulfate, but not by 0.5% cetyltrimethylammonium bromide. In MeOH soln. I was stabilized for 5 days by 2% polyethylene glycol 1000, but not completely by 0.5% polyethylene glycol 900 sorbitan monooleate. In the presence of 5% polyethylene glycol 1400 stearate, the decompn. rate of I increased with temp.
- IT 9004-99-3
 RL: BIOL (Biological study)
 (phenyl salicylate stability in relation to)
 RN 9004-99-3 HCAPLUS
- CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI) (CA INDEX NAME)

=> d bib abs hitstr 12

L40 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2001 ACS 1968:418088 HCAPLUS AN 69:18088 DN ΤI Food additives. Sanitizing solutions ΑU Fed. Regist. (1968), 33, 7684, 24 May 1968 CODEN: FEREAC so DT Journal LA English An aq. soln. of I, butoxy monoether of mixed (ethylene-propylene) polyalkylene glycol with min. av. mol. wt. of 2400, and .alpha.-lauroyl-.omega.-hydroxypoly(oxyethylene) with an av. of 8-9 moles of ethylene oxide and an av. mol. wt. of 400, together with adjuvants may be used under the Federal Food, Drug, and Cosmetic Act as a sanitizing soln. on food processing equipment and utensils that contact food and on beverage containers except those used for milk. The soln. must contain 25 ppm. titratable I. IT 9004-81-3 RL: BIOL (Biological study) (sanitizing solns. contg., standards for) RN 9004-81-3 HCAPLUS Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxododecyl)-.omega.-hydroxy- (9CI) CN (CA INDEX NAME)

=> d bib abs hitstr 13

ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2001 ACS L40

1967:405685 HCAPLUS

DN

Effect of adjuvants on drug preparations. XVI. The effect of ΤI the hydrophilic-lipophilic equilibrium (HLB-value) of surfactants on the release and activity of antibacterial compounds

Thoma, Karl

CS Univ. Munich, Munich, Ger.

Arch. Pharm. Ber. Dtsch. Pharm. Ges. (1967), 300(1), 31-8 SO CODEN: APBDAJ

DT Journal

LA

German cf. CA 66: 98459s. The effect of nonionized surfactants on antiseptic ointments, solns., and preservatives was studied. No significant relation was found between HLB values and the influence of the compd. on the activity of (.beta.-phenoxyethyl)dimethyldodecylammonium bromide (I), 1-hexadecylpyridinium chloride (II), di-Na 2,7-dibromo-4-(hydroxymercuri)fluorescein (III), and Na methylmercurithiosalicylate (IV). The addn. of ethers of polyethylene glycols (PEG), PEG 250 lauryl ether (V), PEG 900 stearyl ether (VI), PEG 1400 stearyl ether (VII) to I and III in ointments and solns. reduced the antibacterial activity of I and III against Staphylococcus aureus SG 511. The invert soaps, PEG sorbitan monolaurate (VIII), PEG sorbitan stearate (IX), PEG sorbitan trioleate (X), PEG 400 stearate (XI), PEG 900 stearate (XII), and PEG 2200 stearate (XIII) produced a very strong decrease in availability of I in ointments and aq. solns. The availability of III in ointments was reduced by VIII-XIII but aq. solns. of III were unaffected. The diffusion of I and III was not dependent on the HLB value of the additive. The bactericidal activity of II was changed by less than 1% XII so that II was bacteriostatic; bacteriostatic activity was lost above 5% XII. V, VIII, and sucrose monolaurate (XIV) acted similarly. IV was unaffected by V-XIII. The effects of V-XIII are not due to their structure (PEG 1000 is indifferent towards invert soaps but is strongly impaired by XIV) but is caused by the existence of a 2nd pseudophase in the form of micelles of surfactant.

9004-99-3

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(antibiotic activity response to)

9004-99-3 HCAPLUS RN

Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$\label{eq:Me-CH2} \texttt{Me-(CH2)_{16}-C} \overset{\texttt{O}}{\underset{\texttt{I}}{\text{C}}} - \texttt{CH}_{2} - \texttt{CH}_{2} - \texttt{CH}_{2} - \texttt{DH}_{2}$$

TΨ 32127-87-0

RL: BIOL (Biological study)

(bactericidal activity of ointments and)

32127-87-0 HCAPLUS

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=> d bib abs hitstr 1
     ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2001 ACS
     2001:355059
AN
                 HCAPLUS
DN
     134:357576
     Preparation of mixed micellar delivery system for pharmaceutical
ТT
     proteins
ΙN
     Modi, Pankaj
PΑ
     Generex Pharmaceuticals Inc., Can.
     U.S., 13 pp., Cont.-in-part of U.S. Ser. No. 21,114.
SO
     CODEN: USXXAM
DΤ
     Patent
     English
FAN.CNT 4
     PATENT NO.
                       KIND DATE
                                             APPLICATION NO.
                                                              DATE
ΡI
     US 6231882
                       В1
                             20010515
                                             US 1998-216733
                                                               19981221
     US 6017545
                        Α
                             20000125
                                             US 1998-21114
                                                               19980210
     BR 9804295
                       Α
                             20000328
                                             BR 1998-4295
                                                               19981027
                             19990819
                                             WO 1999-CA106
                                                               19990205
     WO 9940932
                       Α1
         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9925053
                       A1
                             19990830
                                             AU 1999-25053
                                                               19990205
                                             EP 1999-904638
                                                               19990205
     EP 1053011
                        Α1
                             20001122
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     US 6221378
                             20010424
                                             US 1999-386285
                                                              19990831
                             19980210
PRAI US 1998-21114
                        Α2
     US 1998-216733
                        Α
                             19981221
     WO 1999-CA106
                       W
                             19990205
     A mixed micellar pharmaceutical formulation includes (1) a
     micellar proteinic pharmaceutical agent, i.e., heparin, hirulog,
     hirudin, interferons, interleukins, cytokines, and polyclonal antibodies,
     chemotherapeutic agents, glycoproteins, bacterial toxoids, hormones,
     antibiotics, platelet inhibitors, DNA, RNA, antisense oligonucleotides
     steroids, hypnotics, and pain killers, e.t.c., (2) an alkali metal C8-22
     alkyl sulfate, (3) alkali metal salicylate, (4) a pharmaceutically
     acceptable edetate and (5) at least one absorption enhancing compds.
     absorption enhancing compds. are selected from the group consisting of
     lecithin, hyaluronic acid, pharmaceutically acceptable salts of hyaluronic
     acid, octylphenoxypolyethoxyethanol, glycolic acid, lactic acid, chamomile
     ext., cucumber ext., oleic acid, linolenic acid, borage oil, evening
     primrose oil, trihydroxy oxo cholanylglycine, glycerin, polyglycerin,
     lysine, polylysine, triolein and mixts. thereof. The amt. of each
     absorption enhancing compd. is present in a concn. of 1-10% by wt. of the
     total formulation, and the total concn. of absorption enhancing compds.
     are < 50% by wt. of the formulation. For example, a micellar
     insulin soln. was prepd. using 0.5 g sodium lauryl sulfate, 0.5 g Na salicylate, and 0.25 g disodium edetate dissolved in 10 mL of water.
     this soln. 40 mg (1000 units) of insulin was added and dissolved
     completely while stirring, to give about 100 units/mL insulin oral soln.
     Compared to the injections, oral insulin gave a faster onset of action and
     lowered blood glucose levels without creating hypoglycemic condition. Due
     to the hepatic glucose prodn., there was a rebound effect. This is
     believed to be due to the incomplete absorption of insulin.
IT
     9002-92-0D, Polydocanol, alkyl ethers
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (prepn. of mixed micellar delivery system for proteinic
        drugs)
RN
     9002-92-0 HCAPLUS
CN
     Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA
     INDEX NAME)
```

HO
$$CH_2-CH_2-O$$
 n (CH₂) $11-Me$

RE.CNT 1 RE (1) Modi; US 6017545 2000 HCAPLUS

=> d bib abs hitstr 2

```
ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2001 ACS
     2001:167782 HCAPLUS
AN
DN
     134:227361
ΤI
     Preparation of mixed micellar pharmaceutical delivery system for
     proteinic and other drugs
IN
     Modi, Pankai
     Generex Pharmaceuticals Inc., Can.
PΑ
so
     PCT Int. Appl., 46 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 4
     PATENT NO.
                        KIND DATE
                                                APPLICATION NO. DATE
     _____
                        ----
                               _____
                                                                   20000825
     WO 2001015666
                               20010308
                                               WO 2000-CA1019
PΙ
                         A1
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
              HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
              SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
              YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG 878 B1 20010424 US 1999-386285 19990831
     US 6221378
PRAI US 1999-386285
                               19990831
                         Α
     US 1998-21114
                               19980210
                         A2
                               19981221
     US 1998-216733
                         A2
     A mixed micellar pharmaceutical formulation and process for
     making the formulation are described. The formulation includes a
     micellar proteinic pharmaceutical agent, an alkali metal C8-22
     alkyl sulfate, alkali metal salicylate, a pharmaceutically acceptable
     edetate and at least one absorption enhancing compd. The absorption enhancing compd. is selected from the group consisting of lecithin,
     hyaluronic acid, pharmaceutically acceptable salts of hyaluronic acid,
     octylphenoxypolyethoxyethanol, glycolic acid, lactic acid, chamomile ext.,
     cucumber ext., oleic acid, linolenic acid, borage oil, evening primrose
     oil, trihydroxy oxo cholanylglycine, glycerin, polyglycerin, lysine,
     polylysine, triolein and mixts. thereof. The amt. of each absorption
     enhancing compd. is present in a concn. of 1-10% by wt.; the total
     formulation, and the total concn. of absorption enhancing compds. are <
     50% by wt. of the formulation. Preferably, the formulation is
     administered, in combination with a propellant, to the buccal cavity,
     using a metered dose dispenser, which is also described. For example, an oral drops were prepd. using 0.5 g sodium lauryl sulfate, 0.5 g sodium
     salicylate and 0.25 g disodium edetate dissolved in 10 mL of water. To
     this soln. 40 mg (1000 units) of insulin was added and dissolved
     completely while stirring, to give about 100 units/mL insulin soln.
     Compared to the injection method, oral insulin gives a faster onset of
     action and lowers blood glucose levels without creating hypoglycemic
     condition. Due to the hepatic glucose prodn., there was a rebound effect.
     This is believed to be due to the incomplete absorption of insulin.
     9002-92-0, Polyoxyethylene lauryl ether 9002-92-0D,
     Polydocanol, alkyl ethers
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (prepn. of mixed micelles for oral delivery of proteinic and
        other drugs)
     9002-92-0 HCAPLUS
RN
     Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA
CN
     INDEX NAME)
HO - CH<sub>2</sub> - CH<sub>2</sub> - O - (CH<sub>2</sub>)<sub>11</sub> - Me
```

pod above

9002-92-0 HCAPLUS
Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA RN CN INDEX NAME)

HO
$$CH_2-CH_2-O$$
 n $(CH_2)_{11}-Me$

RE.CNT 6

RE

- (1) Astra Ab; WO 9619197 A 1996 HCAPLUS
 (2) Genentech Inc; WO 9426302 A 1994 HCAPLUS
 (3) Generex Pharm Inc; WO 0037051 A 2000 HCAPLUS
 (4) Modi, P; WO 9636352 A 1996 HCAPLUS
 (5) Modi, P; WO 9940932 A 1999 HCAPLUS

- ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> d bib abs hitstr 3
     ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2001 ACS
     2001:63806 HCAPLUS
AN
DN
     134:136684
     Biodegradable poly(alkylene oxide)-poly(p-dioxanone) block copolymer
ΤI
     soluble in organic solvents, and drug delivery composition comprising same
IN
     Seo, Min-Hyo; Choi, In-Ja
     Samyang Corporation, S. Korea
     PCT Int. Appl., 35 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                        KIND DATE
                                               APPLICATION NO. DATE
     WO 2001005379
                              20010125
                                               WO 2000-KR779
                                                                 20000718
PΤ
                        A1
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
              HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
              LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
              SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG 29269 A 19990720
PRAI KR 1999-29269
     The present invention relates to a biocompatible and biodegradable block
     copolymer of poly(alkylene oxide) and poly(p-dioxanone) (PDO), which is
     sol. in org. solvents, for delivery of peptides, proteins, antitumor agents, antiphlogistic anodyne agents, antibiotics, antibacterials,
     hormones, genes, and vaccines. Drug delivery compns. comprise
     microspheres, microcapsules, films, strips, fibers, gels, sols,
     nanospheres, nanocapsules, and micelles. For example, 5 g of
     poly(ethylene glycol) monomethyl ether and 10 g of 1,4-dioxane-2-one
     reacted in presence of 4.06 mg of stannous octoate to obtain a mPEG-PDO
     diblock copolymer with the mPEG content of 46.3 wt.%. The mPEG-PDO
     diblock copolymer (0.85 g) was dissolved in 2 mL of dichloromethane and
     0.15~\mbox{g} of ofloxacin was suspended therein. The suspension was added to a
     1 wt.% polyvinyl alc. aq. soln. and stirred at 1200
     rpm to obtain a microsphere soln. The soln. was freeze-dried to give
     microspheres having an av. particle size of 10 .mu. and contg. 14.6%
     ofloxacin.
ΙT
     321658-19-9P
     RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
         (diblock; biodegradable poly(alkylene oxide)-poly(p-dioxanone) block
         copolymer sol. in org. solvents for drug delivery systems)
RŃ
     321658-19-9 HCAPLUS
     1,4-Dioxan-2-one, polymer with .alpha.-methyl-.omega.-hydroxypoly(oxy-1,2-
     ethanediyl), block (9CI) (CA INDEX NAME)
     CM
     CRN
           9004-74-4
           (C2 H4 O)n C H4 O
     CMF
     CCI
           PMS
        -сн<sub>2</sub>-сн<sub>2</sub>-о
     CM
```

CRN 3041-16-5 CMF C4 H6 O3

- RE.CNT 2 RE (1) Ethicon; US 5019094 1991 HCAPLUS (2) United States Surgical Corp; US 5522841 1996 HCAPLUS

```
=> d bib abs hitstr 4
     ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2001 ACS
AN
     2000:741894 HCAPLUS
DN
     133:313641
TΙ
     Lipid aggregate-forming compositions and their uses
     Leigh, Steven; Leigh, Mathew Louis Steven
IN
     Phares Pharmaceuticals Research N.V., Neth. Antilles
     PCT Int. Appl., 40 pp.
     CODEN: PIXXD2
DТ
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                        KIND DATE
                                                APPLICATION NO.
     WO 2000061113
                         A1
                               20001019
                                                WO 2000-GB1361
                                                                    20000411
PΤ
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
              CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
              ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
              LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
              ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
              DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
              CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI GB 1999-8309
                         Α
                               19990412
     Formulations are provided which contain at least one micelle
      -forming monoacyl membrane lipid either alone or preferably in combination
     with one or more bilayer-forming diacyl membrane lipids. The compns. are
     characterized by the presence of an effective amt. of the monoacyl component and a lipophilic component dissolved or dispersed in a
     hydrophilic medium in an amt. effective to convert the compn. into a liq.,
     gel or semi-solid which has the property of yielding dispersed lipid
     aggregates upon contact or further diln. with an ag. medium. Particular
     liq. pharmaceutical compns. comprise: (a) a mixt. of membrane lipids which comprises a micelle-forming lipid and preferably a
     bilayer-forming lipid; (b) a lipophilic component; (c) at least one
     hydrophilic medium to mobilize the lipids; and optionally (d) a biol.
     active compd. Other compns. comprise water in an amt. which is effective
     to hydrate the lipid mixt., and a biol. active compd. Enzyme modified lecithin 40, Miglyol 810 10, vitamin A propionate 5 parts were dissolved
      in ethanol 20, propylene glycol 10, and water 5. The compn. was heated
     and dild. to obtain a clear yellow dispersion of microscopic lipid
     aggregates.
     111-90-0
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (drug carriers contg. micelle-forming membrane lipids and
         bilayer-forming lipids and other ingredients)
     111-90-0 HCAPLUS
     Ethanol, 2-(2-ethoxyethoxy)- (8CI, 9CI) (CA INDEX NAME)
EtO- CH2- CH2- O- CH2- CH2- OH
RE.CNT 5
RE
(1) Cipla Limited; EP 0760237 A 1997 HCAPLUS
(2) Hoechst Ag; EP 0649660 A 1995 HCAPLUS
(3) Leigh, M; WO 9858629 A 1998 HCAPLUS
(4) Leigh, M; WO 9944642 A 1999 HCAPLUS
```

(5) Vesifact Ag; EP 0956853 A 1999 HCAPLUS

```
=> d bib abs hitstr 5
      ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2001 ACS
L47
      2000:441602 HCAPLUS
ΑN
DN
      133:63985
ΤI
      Aerosol formulations for buccal and pulmonary application
      Modi, Pankaj
PΑ
      Generex Pharmaceuticals Inc., Can.
      PCT Int. Appl., 46 pp.
SO
      CODEN: PIXXD2
DT
      Patent
LA
      English
FAN.CNT 1
      PATENT NO.
                          KIND DATE
                                                  APPLICATION NO. DATE
                                                  WO 1999-CA1231
      WO 2000037051
                          A1
                                 20000629
PΙ
                                                                      19991216
          W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
               CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
               MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
               AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1998-113239
                          P
                                 19981221
      US 1999-251464
                                19990217
                                19990831
      US 1999-386284
                          Α
      A mixed micellar aerosol pharmaceutical formulation includes a
      micellar protein pharmaceutical agent, an alkali metal lauryl
      sulfate, at least three micelle forming compds., a phenol and a
      propellant. The micelle forming compds. are selected from the
      group consisting of lecithin, hyaluronic acid, pharmaceutically acceptable salts of hyaluronic acid, glycolic acid, lactic acid, chamomile ext.,
     cucumber ext., oleic acid, linoleic acid, linolenic acid, monoolein, monooleates, monolaurates, borage oil, evening of primrose oil, menthol,
      trihydroxy oxocholanyl glycine and pharmaceutically acceptable salts
      thereof, glycerin, polyglycerin, lysine, polylysine, triolein,
      polyoxyethylene ethers and analogs thereof, polydocanol alkyl ethers and
      analogs thereof, chenodeoxycholate and deoxycholate. The amt. of each
      micelle forming compd. is present in a concn. of from 1 to 20
      wt./wt.% of the total formulation, and the total concn. of micelle
      forming compds. are less than 50 wt./wt.% of the formulation.
      propellant, e.g., a fluorocarbon propellant, provides enhanced absorption
      of the pharmaceutical agent, particularly in the buccal cavity. An
      example was given using insulin as the active ingredient.
      9002-92-0
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
          (aerosol formulations for buccal and pulmonary application)
      9002-92-0 HCAPLUS
RN
CN
      Poly(oxy-1,2-ethanediy1), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA
      INDEX NAME)
     CH2-CH2-O- (CH2)11-Me
RE.CNT 6
RF.
(1) Alliance Pharma; WO 9640057 A 1996 HCAPLUS
(2) Biozone Lab Inc; WO 9742938 A 1997 HCAPLUS
(3) Chandarana, S; WO 9636352 A 1996 HCAPLUS
(4) Leigh, S; US 5004611 A 1991 HCAPLUS
(5) Modi; P; WO 9940932 A 1999 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

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=> d bib abs hitstr 6
L47
     ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2001 ACS
     1999:795833 HCAPLUS
AN
     132:26803
DN
ΤI
     Method for preparing virus-safe pharmaceutical compositions
     Tolo, Hannele; Parkkinen, Jaakko
PA
     Suomen Punainen Risti Veripalvelu, Finland
     PCT Int. Appl., 23 pp.
     CODEN: PIXXD2
DT
     Patent
     English
FAN.CNT 1
     PATENT NO.
                        KIND DATE
                                               APPLICATION NO.
                                                                  DATE
                              19991216
                                               WO 1999-FI505
PΙ
     WO 9964441
                         A1
                                                                  19990609
         W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
              DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
              JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
              MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
              MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
              ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                              19991211
                                               FI 1998-1337
     FI 9801337
                         Α
                                                                  19980610
     AU 9947834
                         A1
                              19991230
                                              AU 1999-47834
                                                                  19990609
                              20010328
                                               EP 1999-931279
     EP 1086120
                         A1
                                                                  19990609
         R: AT, CH, DE, ES, FR, GB, LI, NL, SE
                              19980610
PRAI FI 1998-1337
                         Α
     WO 1999-FI505
                         W
                              19990609
     The present invention concerns a method of prepg. pharmaceutical compns.
     of a biol. active proteins, in particular multicomponent interferon
     compns. The invention comprises the steps of adding to a soln. of the
     protein a non-ionic detergent in an efficient amt. to provide an extended
     shelf-life of the pharmaceutical compn.; subjecting the soln. contg. the
     nonionic detergent to filtration on a virus removal filter with
     a pore size of 10 to 40 nm; and recovering the filtrate. The method gives
     rise to, e.g., a virus-safe multicomponent .alpha.-interferon
     compn., comprising a nonionic detergent as a stabilizer in an amt.
     exceeding the crit. micellar concn. of the detergent and being
     essentially free from substances retained on a virus-filter
     having high virus retentive capacity.
ΙT
     9002-92-0, Brij 35
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
         (prepg. virus-safe pharmaceutical compns.)
     9002-92-0 HCAPLUS
CN
     Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA
     INDEX NAME)
        CH<sub>2</sub>-CH<sub>2</sub>-O (CH<sub>2</sub>)<sub>11</sub>-Me
```

RE.CNT RE

- (1) Dr Karl Thomas Gmbh; EP 0231816 A2 1987 HCAPLUS(2) Interferon Sciences, Inc A Delaware Corporation; EP 0152345 A2 1985 HCAPLUS
- (3) Seitz-Filter-Werke Gmbh Und Co; EP 0571871 A2 1993 HCAPLUS

19990503

```
=> d bib abs hitstr 7
     ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2001 ACS
     1999:686550 HCAPLUS
AN
DN
     131:303230
ΤI
     Customization of hair care formulations
IN
     Rath, Maureen L.; Hlavac, Wallace R.
     Tiro Industries Incorporated, USA
     U.S., 13 pp., Cont. of U.S. Ser. No. 969,492.
     CODEN: USXXAM
DT
     Patent
LA
     English
FAN.CNT 2
     PATENT NO.
                     KIND DATE
                                          APPLICATION NO.
     US 5972322
                           19991026
                                          US 1999-304246
PΤ
                      Α
     US 5993792
                      Α
                           19991130
                           19971113
```

US 1997-969492 19971113 PRAI US 1997-969492 The invention provides a system for prepg. a hair shampoo, conditioner, and styling compn., wherein each system is composed of sep. components that can be combined as desired by the user to provide customized hair care formulations. The systems include a water-thin base compn., a thickening compn., and optional enhancing additives, wherein each compn. is sep. packaged. The viscosity of the end-product shampoo, conditioner, or styling compn. can be varied, from a thick, pourable liq. to a thicker, pasty material depending on the amt. of thickener that is added to the base. An optional styling compn. was prepd. by combining the ingredients shown below. The product contained deionized water 75.0, Germaben II 1.0, 20% aq. soln. of Gafquat 755N 8.0, and 50% aq . soln. of PVP/VA W-35 16.0%. 9002-92-0, Laureth-23 9004-99-3D, C16-18- and iso-C16-18-alkyl ethers 24938-91-8, Salcare-SC95

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (customization of hair care formulations)

9002-92-0 HCAPLUS BN

Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA

$$HO = \begin{bmatrix} CH_2 - CH_2 - O \end{bmatrix}_n (CH_2)_{11} - Me$$

RN 9004-99-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI) (CA INDEX NAME)

Me-
$$(CH_2)_{16}$$
- C- CH₂- CH₂- CH₂- OH

RN 24938-91-8 HCAPLUS

Poly(oxy-1,2-ethanediyl), .alpha.-tridecyl-.omega.-hydroxy- (9CI) (CA

$$HO - CH_2 - CH_2 - O - I_n (CH_2)_{12} - Me$$

RE.CNT 15 .

(1) Anon; WO 9725963 1997 HCAPLUS

- (2) Casperson; US 5376146 1994 HCAPLUS
 (3) Ciaudelli; US 5084270 1992 HCAPLUS
 (4) Darkwa; US 5077042 1991 HCAPLUS
 (5) Darkwa; US 5293885 1994 HCAPLUS
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d bib abs hitstr 8

ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2001 ACS

1999:655903 HCAPLUS AN

131:285527 DN

TΙ Manufacture of the pancreatic islet autoantigen GAD65 in methylotrophic

Raymond, Christopher K.; Bukowski, Thomas R.; Bishop, Paul D.

PA

ZymoGenetics, Inc., USA
U.S., 25 pp., Cont.-in-part of U.S. Ser. No. 703,807.
CODEN: USXXAM SO

דת Patent

English LA

FAN.CNT 7

PATENT NO.	KIND	DATE	APPLICATION NO. DATE
PI US 5965389	Α	19991012	US 1996-747108 19961108
US 5716808	Α	19980210	US 1996-703809 19960826
US 5955349	Α	19990921	US 1996-703807 19960826
CA 2237039	AA	19970515	CA 1996-2237039 19961108
CA 2237120	AA	19970515	CA 1996-2237120 19961108
US 5888768	Α	19990330	US 1997-932924 19970918
PRAI US 1995-639	7 P	19951109	
US 1996-703	807 A2	19960826	
US 1996-703	809 A2	19960826	

AB A method of manufg. a biol. active form of the GAD65 autoantigen of pancreatic islets by expression of the gene in methylotrophic yeasts is described. The GAD65 autoantigen is a glutamate decarboxylase with several disulfide bridges and two palmitoylated sites that aggregates readily in aq. soln. A methanol-inducible promoter from, for example, an alc. oxidase gene, such as Pichia pastoris AOX1, can be used to regulate GAD65 expression. The GAD65 has high specific activity and retains antigenic characteristics of the native mol. that are essential to immunol. assays and therapeutic protocols. Development of a non-secretory expression system for Pichia methanolica using the promoters of alc. utilization genes (AUG1 and AUG2) and ADE2 auxotrophic marker is also described. Purifn. of the enzyme from producer strains using detergent phase sepn. with Triton X114 and ion-exchange chromatog. is also demonstrated.

TT **9002-93-1**, Triton X-100

RL: BUU (Biological use, unclassified); MOA (Modifier or additive use); BIOL (Biological study); USES (Uses)

(in solubilization and purifn. of GAD65; manuf. of pancreatic islet autoantigen GAD65 in methylotrophic yeasts)

9002-93-1 HCAPLUS RN

CN $\texttt{Poly}(\texttt{oxy-1}, 2-\texttt{ethanediyl}), \quad .\texttt{alpha.-[4-(1,1,3,3-\texttt{tetramethylbutyl})phenyl]-}$.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me}_3\text{C-CH}_2\text{-C} \\ \text{Me} \end{array}$$

RE.CNT 29

RE

- (1) Anon; EP 0299108 1989 HCAPLUS
- (2) Anon; EP 0341746 1989 HCAPLUS
- (3) Anon; WO 92/05446 1992 HCAPLUS
- (4) Anon; WO 92/20811 1992 HCAPLUS (5) Anon; WO 95/04137 1995 HCAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> d bib abs hitstr 9
L47
     ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2001 ACS
     1999:529037 HCAPLUS
AN
DN
     131:161639
TI
     Mixed micellar pharmaceutical delivery system containing
     proteins
IN
     Modi, Pankaj
PA
     Can.
SO
     PCT Int. Appl., 55 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 4
     PATENT NO.
                        KIND DATE
                                               APPLICATION NO.
                                                                  DATE
     WO 9940932
                         A1
                               19990819
                                               WO 1999-CA106
                                                                   19990205
          W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
              KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
              NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,
                                                                   ТJ,
                                                                        TM,
                                                                            TR, TT,
              UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
              CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 6017545
                               20000125
                                               US 1998-21114
                                                                   19980210
     US 6231882
                               20010515
                                               US 1998-216733
                                                                   19981221
                               19990830
                                               AU 1999-25053
                                                                   19990205
     AU 9925053
                         Α1
                                               EP 1999-904638
     EP 1053011
                         A1
                               20001122
                                                                  19990205
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, FI
PRAI US 1998-21114
                               19980210
     US 1998-216733
                         Α
                               19981221
     WO 1999-CA106
                         W
                               19990205
AB
     A mixed micellar pharmaceutical formulation includes a
     micellar proteinic pharmaceutical agent, an alkali metal C8-22
     alkyl sulfate, alkali metal salicylate, a pharmaceutically acceptable
     edetate and at least one absorption enhancing compds. The absorption
     enhancing compds. are selected from the group consisting of lecithin,
     hyaluronic acid, pharmaceutically acceptable salts of hyaluronic acid,
     octylphenoxypolyethoxyethanol, glycolic acid, lactic acid, chamomile ext.,
     cucumber ext., oleic acid, linolenic acid, borage oil, evening primrose
     oil, trihydroxy oxo cholanylglycine, glycerin, polyglycerin, lysine, polylysine, triolein and mixts. thereof. The amt. of each absorption
     enhancing compd. is present in a concn. of from 1 to 10 wt./wt.% of the
     total formulation, and the total concn. of absorption enhancing compds.
     are less than 50 wt./wt.% of the formulation. Insulin was added to a
     buffer soln. contg. sodium lauryl sulfate 0.5, sodium salicylate 0.5, disodium edetae 0.25 g, and water 10 mL and mixed to form \tt micellar
                To a soln. of 100 mg phosphatidylcholine-H in 10 mL 50% ethanol
     was added 16 mg (400 units) of micellar insulin soln. To this
     was added 0.6 mL of sodium hyaluronate and 0.2 mL of 2% menthol soln.
     contg. 3% sorbitol. Type II diabetic human volunteers were given 30 units
     (about 20 drops) of the above oral soln. (3 times the injection dose).
     The oral insulin formulation was comparable to the injected insulin in
     lowering blood glucose level.
     9002-92-0, Polidocanol
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (mixed micellar pharmaceutical delivery system contg.
         proteins)
RN
     9002-92-0 HCAPLUS
     Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI)
     INDEX NAME)
HO - CH_2 - CH_2 - O - CH_2)_{11} - Me
```

RE.CNT 4

- RE.
 (1) Baeckstroem, K; WO 9619197 A 1996 HCAPLUS
 (2) Genentech Inc; WO 9426302 A 1994 HCAPLUS
 (3) Modi, P; WO 9636352 A 1996 HCAPLUS
 (4) Yamamoto, A; Journal of Controlled Release 1996, V41(1), P57

```
=> d bib abs hitstr 10
L47
     ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2001 ACS
     1998:677836 HCAPLUS
AN
     129:306510
DN
ΤI
     Stabilized human papillomavirus antigen formulations that resist
     aggregation
IN
     Sanyal, Gautum; Volkin, David B.; Shi, Li
     Merck & Co., Inc., USA
PA
     PCT Int. Appl., 72 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                        KIND
                              DATE
                                               APPLICATION NO.
                                                                 DATE
                        ----
     WO 9844944
                        A2
                              19981015
                                               WO 1998-US6825
                                                                 19980407
                              19981230
     WO 9844944
                        A3
         W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW,
              HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA,
              US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
              CM, GA, GN, ML, MR, NE, SN, TD, TG
     ZA 9802950
                              19981019
                                               ZA 1998-2950
                                                                 19980407
     AU 9869533
                              19981030
                                               AU 1998-69533
                                                                 19980407
                              20000126
                                               EP 1998-915319
     EP 973546
                        A2
                                                                 19980407
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
     NO 9904879
                        Α
                              19991207
                                               NO 1999-4879
                                                                 19991007
PRAI US 1997-42808
                              19970408
     GB 1997-9351
                              19970507
     WO 1998-US6825
                              19980407
AB
     Human papillomavirus (HPV) antigen formulations are disclosed
     which prevent protein aggregation and show prolonged stability as
     aq. solns. These formulations comprise a salt (such as
     sodium chloride) and a non ionic surfactant (Polysorbate 80 such as Tween
     80) in physiol. acceptable concns.
IT
     9002-93-1, Triton x 100
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
         (stabilized human papillomavirus antigen formulations that
        resist aggregation)
     9002-93-1 HCAPLUS
RN
     \texttt{Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-}
CN
     .omega.-hydroxy- (9CI) (CA INDEX NAME)
```

Me Me
$$3C-CH_2-CH_2$$
 OH Me

=> d bib abs hitstr 11

- L47 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2001 ACS
- AN 1998:617622 HCAPLUS
- DN 129:329667
- TI Determination of the non-ionic detergent insolubility and phosphoprotein associations of glycosylphosphatidylinositol-anchored proteins expressed on T cells
- AU Solomon, Keith R.; Mallory, Mark A.; Finberg, Robert W.
- CS Infectious Disease Unit, Dana-Farber Cancer Institute, Boston, MA, 02115,
- SO Biochem. J. (1998), 334(2), 325-333 CODEN: BIJOAK; ISSN: 0264-6021
- PB Portland Press Ltd.
- DT Journal
- LA English
- AΒ Glycosylphosphatidylinositol (GPI)-anchored proteins are poorly solubilized in non-ionic detergents such as Triton X-100 and Nonidet P40, but are easily solubilized by detergents with high crit. micelle concns. such as octylglucoside. This soly. profile has been suggested to be due to the localization of GPI-anchored proteins to lipid microdomains rich in cholesterol and sphingolipids. Addnl., GPI-anchored proteins expressed on hemopoietic cells have been shown to assoc. with src-family tyrosine kinases and heterotrimeric G proteins. Despite these observations, the non-ionic detergent insoly. of GPI-anchored proteins on hemopoietic cells has not been quantified nor has a relation between the non-ionic detergent insoly. of these proteins and their assocn. with signal-transduction mols. been identified. Here the authors show that GPI-anchored proteins found on T-cell tumors and activated T cells, although significantly more insol. then transmembrane proteins, are not uniform in their detergent insoly. Whereas CD59 was between 4\$ and 13\$ sol., CD48 was between 13\$ and 25\$ sol., CD55 was between 20\$ and 30\$ sol., and CD109 was between 34\$ and 75\$ sol. The ability of these GPI-anchored proteins to assoc. with phosphoproteins was correlated with their detergent insoly.: the more detergent-insol. that a GPI-anchored protein was, the greater the level of phosphoprotein assocns. These expts. reveal a relation between non-ionic detergent insoly. and assocn. with signal-transduction mols. and suggest a cause-and-effect relation between these two properties. In total, these expts. support the hypothesis that the assocn. of GPI-anchored proteins with signaling mols. is due to their sorting to lipid microdomains.
- IT 9002-93-1, Triton X-100
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (T-cell GPI-anchored protein soly. in)
- RN 9002-93-1 HCAPLUS
- CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl].omega.-hydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me} & \text{Me} \end{array}$$

```
=> d bib abs hitstr 12
```

L47 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:71204 HCAPLUS

DN 128:145333

TI Preserving infectious recombinant viruses as aqueous suspensions in sucrose solutions for therapeutic use

IN Sene, Claude

PA Transgene S.A., Fr.; Sene, Claude

SO PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DT Patent

LA French

FAN CNT 1

PAN.	PATENT NO.	KIND DA	ATE	APPLICATION NO.	DATE
PI			9980122	WO 1997-FR1308	19970715
		CH, DE, I			LU, MC, NL, PT, SE
	FR 2751343	A1 19	9980123	FR 1996-8851	19960716
	FR 2751343	B1 19	9981218		
	CA 2232604	AA 19	9980122	CA 1997-2232604	19970715
	AU 9736986	A1 19	9980209	AU 1997-36986	19970715
	AU 711409	B2 19	9991014		
	EP 853660	A1 19	9980722	EP 1997-933740	19970715
	R: AT, BE,	CH, DE, I	DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,
	IE, FI				
	JP 2000500026	T2 20	0000111	JP 1998-505691	19970715
PRAI	FR 1996-8851	19	9960716		

WO 1997-FR1308 19970715

AB Method for preserving infectious recombinant viruses, particularly adenovirus, in frozen or liq. form using a buffered aq. soln. contg. saccharose at 0.75-1.5 M (preferably 1M) and the therapeutic use of such a suspension are described. The use of sucrose as a stabilizer avoids the use of glycerol, which can be irritant to some mucous membranes, e.g. the lungs, and increase the storage lifetime of the virus at 4.degree. or -20.degree. to >6 mo without significant loss of titer. The medium is buffered and the virus is also stabilized with a monovalent and divalent cation. Nonionic detergents may also be added. Optimization expts. for stabilization of an adenovirus are reported. Conditions under which titers were retained with less than an order of magnitude loss (at

IT 9002-93-1, Triton X-100

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preserving infectious recombinant viruses as aq. suspensions in sucrose solns. for therapeutic use)

RN 9002-93-1 HCAPLUS

CN Poly(oxy-1,2-ethanediy1), .alpha.-[4-(1,1,3,3-tetramethylbuty1)pheny1]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me} & \text{Me} \end{array}$$

.apprx.1010 pfu/mL) were obtained.

⇒> d bib abs hitstr 13

L47 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2001 ACS

AN 1996:130069 HCAPLUS

DN 124:211827

TI Propellant-driven aerosols of proteins

AU Brown, Alan R.

CS Dep. of Diagnostic Medicine/Pathobiology, Kansas State Univ., Manhattan, KS, 66506, USA

SO Aerosol Sci. Technol. (1996), 24(1), 45-56 CODEN: ASTYDQ; ISSN: 0278-6826

DT Journal

LA English

The protein bovine .gamma.-globulin was combined with surfactants, AB suspended in a di-Me ether propellant, and delivered through metered-dose aerosol valves to produce small particle aerosols of protein. A fraction of the protein particles was of respirable size (.ltoreq.4 .mu.m aerodynamic diam.) as detd. by cyclone or impactor aerosol sampling. Protein/surfactant molar rations of 1:1000 to 2000 produced the greatest percentage of respirable-sized protein particles. Excessive surfactant reduced the fraction of respirable-size particles, whereas too little surfactant limited the suspension of protein in liquefied propellant. protein/surfactant densities in propellant increased the fraction of respirable-sized protein particles in aerosols, with 28-36% of aerosolized protein of respirable size when protein concns. were 0.2 mg/mL of propellant. Protein densities of up to 4 mg/mL in propellant could be delivered as aerosols, but with a reduced respirable fraction. Aq . ${\tt solns.}$ of proteins at concns. of 1 to 2 ${\tt mg/mL}$ combined with surfactants and then lyophilized to remove all water were aerosolized most effectively when suspended in propellant. Addn. of glass beads or aerosol vials enhanced the dispersion of agitated protein/surfactant suspensions and improved protein aerosolization. Addn. of 2-4% ethanol in propellant increased the fraction of respirable-size aerosol particles of protein particles in aerosols. The potential of propellant-driven aerosols for delivering therapeutic enzymes and antibodies, immuno-modulating cytokines, and immunizing vaccines to the respiratory tract is discussed.

IT **9002-92-0**, Laureth-9

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (propellant-driven aerosols of proteins)

RN 9002-92-0 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$HO = \begin{bmatrix} CH_2 - CH_2 - O \end{bmatrix}_n (CH_2)_{11} - Me$$

=> d bib abs hitstr 14

- L47 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2001 ACS
- AN 1994:663544 HCAPLUS
- DN 121:263544
- TI Propellant-driven aerosols of functional proteins as potential therapeutic agents in the respiratory tract
- AU Brown, Alan R.; Slusser, Joyce G.
- CS Department of Pathology and Microbiology, College of Veterinary Medicine, Kansas State University, Manhattan, KS, 66506, USA SO Immunopharmacology (1994), 28(3), 241-57
- SO Immunopharmacology (1994), 28(3), 241-5 CODEN: IMMUDP; ISSN: 0162-3109
- DT Journal
- LA English
- Aerosols of respirable-sized particles of functional proteins were delivered by volatile propellant from metered-dose aerosol canisters. enzyme alk.-phosphatase and a monoclonal antibody were lyophilized with surfactant and suspended in the aerosol propellant dimethylether. As much as 20 .mu.g of functional protein, assessed by enzyme function or antibody binding activity, was delivered per 40 .mu.l of released propellant. Up to 25% of the protein was of respirable size (.ltoreq.4 .mu.m mass median aerodynamic diam.) when aerosolized proteins were sampled with a Casella cyclone. Respirable particles were derived from visible surfactant/protein complexes suspended in the liquefied propellant and from propellant-sol., nonsedimentable, surfactant/protein mols. that are probably reverse micelles. 10-14 days of propellant exposure in dimethylether increased protein soly. in the propellant, increased the total protein aerosolized and maintained or increased the quantity of respirable-sized protein mols., as compared to the day aerosol vials were charged with propellant. Scanning electron microscopic studies of the respirable-sized protein/surfactant particles showed that they ranged in size from 0.07 to 3.25 .mu.m in diam., and they appeared to be chain aggregates of spherical subunits, 0.11 to 0.93 .mu.m in diam. This structural motif was common to both proteins. The possibility of delivering immunizing antigens, cytokines, passive antibodies and other therapeutic proteins to the respiratory tract using propellant-driven aerosols is discussed.
- IT 9002-92-0, Laureth 9
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (propellant-driven aerosols of functional proteins for respiratory tract)
- RN 9002-92-0 HCAPLUS

```
=> d bib abs hitstr
L55 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2001 ACS
     1989:512018 HCAPLUS
DN
     111:112018
     Agglutination immunoassay and kit for determination of a multivalent
TΙ
     immune species using a buffered salt wash solution
TN
     Snyder, Brian Anthony; Belly, Robert Troconis
     Eastman Kodak Co., USA
     Eur. Pat. Appl., 9 pp.
     CODEN: EPXXDW
DТ
     Patent
LA
     English
FAN.CNT 8
     PATENT NO.
                       KIND DATE
                                              APPLICATION NO.
                                                                DATE
     EP 280559
                        A2
                              19880831
                                              EP 1988-301654
                                                                19880226
PΤ
     EP 280559
                        A3
                              19900919
                        В1
                              19931020
     EP 280559
         R: CH, DE, FR, GB, LI, SE
     US 4847199
                              19890711
                                              US 1987-19850
                                                                19870227
                        Α
                                              CA 1987-539760
     CA 1308349
                              19921006
                                                                19870616
                        Α1
     JP 63229366
                        Α2
                              19880926
                                              JP 1988-42396
                                                                19880226
PRAI US 1987-19850
                              19870227
    A test kit is used in an agglutination immunoassay to det. a multivalent
     immune species, such as Streptococcus A antigen, in a biol.
     sample. The method includes contacting an aq. soln.
     of the species with an agglutination indicator reagent having receptor
     mols. reactive with the species to form an agglutinate of the reaction
     product of species and receptor. These receptor mols. are bound to
     polymeric particles which contain tracer mols. The resulting agglutinate is captured on a microporous membrane which has an av. pore size which is
     .gtoreq.5 times greater than the av. diam. of the polymeric particles.
     Unagglutinated residual materials are washed through the membrane using a
     wash soln. which has a pH of 5-10 and an ionic strength .gtoreq.0.25.
     Tracer is then detd. either in the agglutinate or in the residual materials. The test kit includes the agglutination indicator reagent, the
     wash soln. and optionally an extn. compn. To prep. an agglutination
     reagent, Oil Red EGN was incorporated into core-shell polymer particles
     composed of a styrene-2-acetoacetoxyethyl methacrylate copolymer core, and
     an m,p-chloromethylsytrene homopolymer shell. Streptococcus A antigen monoclonal antibodies were covalently linked to the
     particles, which were then treated with succinic anhydride. The
     antigen was extd. from a clin. isolate with equal vols. of NaNO2
     (8 m) and citric acid (0.2M) and then neutralized with
     3-(N-morpholino)propanesulfonic acid buffer (2M, pH 7.5) contg. EDTA (75
     mM). A mixt. of NaCl (80 .mu.L, 1M), agglutination reagent (40 .mu.L) and
     extd. antigen (80 .mu.L, .apprx.4.2 .times. 105 CFU/mL) was
     added to the test well of a device contg. a nylon 66 membrane (5 .mu.m),
     incubated 2 min. at 25.degree., and allowed to drain through. Controls
     used distd. H2O and NaCl \tilde{0}.025M as wash solns. The amt. of dye remaining
     on the membrane was measured at 540 nm by reflectance spectrophotometry.
     The 2 controls did not show adequate detention of the dye.
     122458-45-1D, monoclonal antibody conjugates
     RL: ANST (Analytical study)
         (Neisseria gonorrhoeae PIB antigen detn. by agglutination
        test using)
     122458-45-1 HCAPLUS
RN
     1,2-Ethanediol, monoacetate, polymer with 2-chloro-4-ethenyl-1-
     methylbenzene and ethenylbenzene (9CI) (CA INDEX NAME)
     CM
          -1
     CRN 105595-71-9
     CMF C9 H9 C1
```

$$\begin{array}{c} \text{CH} \longrightarrow \text{CH}_2 \\ \text{Me} \\ \text{Cl} \end{array}$$

CM

CRN 542-59-6 CMF C4 H8 O3

 $Aco-CH_2-CH_2-OH$

CM

CRN 100-42-5 CMF C8 H8

 $_{\text{H}_2\text{C}}=\text{CH}-\text{Ph}$

```
=> d bib abs hitstr 1
L58 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2001 ACS
AN
     1998:485461 HCAPLUS
DN
     129:162000
     Core/shell-type microspheres with good controllability of particle size
ΤI
     and their preparation
     Kataoka, Kazunori; Kato, Masao; Nagasaki, Sachio; Ijima, Michihiro;
     Fukuzawa, Sumiyo; Okano, Teruo
     Kataoka, Kazunori, Japan
PA
SO
     Jpn. Kokai Tokkyo Koho, 11 pp.
     CODEN: JKXXAF
DΤ
     Patent
     Japanese
LA
FAN.CNT 1
     PATENT NO.
                       KIND DATE
                                               APPLICATION NO. DATE
     _____
                        ____
                              -----
                                               -----
                       A2 19980728
                                              JP 1996-356630 19961227
     Title microspheres, useful for carriers of drugs, are core/shell-type ones derived from stabilized polymer micelles obtained through
     polymn. of macromers shown as (HPLS-HPBS)-PLZA (HPLS = hydrophilic polymer
     segment; HPBS = hydrophobic polymer segment; PLZA = polymerizable group
     having ethylenically unsatd. double bonds linked to either terminal of
     HPLS or HPBS), whose core regions contain affinity polymers to
     core-forming polymer segments. Their prepn. is also claimed. Thus, a
     block copolymer (prepd. from 2-methoxyethanol 0.76, ethylene oxide 53,
     lactide 58, and methacrylic anhydride 23 g) was mixed with
     dimethylacetamide and V 65 (azobisisovaleronitrile), dialyzed against H2O,
     and polymd. to give stabilized polymer micelles, which was mixed with styrene and V 65 and polymd. to obtain core/shell-type microspheres
     with good controllability of particle size according to styrene addn. amt.
     210842-39-0P
     RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
         (core-shell; prepn. of core/shell-type microspheres with good
         controllability of particle size)
RN
     210842-39-0 HCAPLUS
     1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with ethenylbenzene and oxirane, 2-methoxyethyl ether, block, graft (9CI) (CA INDEX NAME)
     CM
     CRN 109-86-4
     CMF C3 H8 O2
но-сн2-сн2-о-сн3
          2
     CM
     CRN 210760-54-6
     CMF
          (C8 H8 . C6 H8 O4 . C2 H4 O)x
     CCI PMS
     CDES 8:PM, BLOCK, GRAFT
           CRN 100-42-5
           CMF C8 H8
H_2C = CH - Ph
```

CM

CRN 95-96-5

CMF C6 H8 O4 CDES *

CM 5

CRN 75-21-8 CMF C2 H4 O

 $^{\circ}$

```
=> d bib abs hitstr 2
      ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2001 ACS
· L58
      1997:405695 HCAPLUS
 DN
      127:19957
 ΤI
      Fabric conditioning compositions
 IN
      Khoshdel, Ezat; Whaley, Christopher
 PA
      Unilever Plc, UK
      Brit. UK Pat. Appl., 30 pp.
      CODEN: BAXXDU
 DT
      Patent
 LA
      English
 FAN.CNT 1
      PATENT NO.
                          KIND DATE
                                                   APPLICATION NO. DATE
 РΤ
      GB 2304727
                           A1 19970326
                                                  GB 1995-18529
                                                                      19950911
 AΒ
      A fabric conditioning compn. comprises a fabric softening compd. such as
      quaternary ammonium compd. and a soil releasing copolymer
      polyether-polyester comprising (i) monomer units of poly(ethylene glycol)
      and/or capped poly(ethylene glycol); (ii) monomer units of an arom. dicarboxylic acid COArCOO (Ar = a bifunctional arom. group), (iii) monomer
      units, of a polyol having .gtoreq.3 OH groups CH2ACH2O (A = a bifunctional
      group contg. .gtoreq.1 C atom and .gtoreq.1 OH group). The polymer may be formed from polyethylene glycol, terephthalic acid and glycerol. A
      nonionic surfactant may be present as a stabilizer. A typical formulation included 0.005 g polyethylene glycol-glycerol-di-Me terephthalate
      copolymer (no.-av. mol. wt. 1700) added to 0.165 mL aq.
      soln. contg. 14.5% 1,2-bis(hydrogenated tallowoyloxy)-3-
      trimethylammonium propane chloride/fatty acid 6:1.
      186910-35-0 186910-36-1
      RL: MOA (Modifier or additive use); USES (Uses)
          (soil release agents for fabric conditioning compns. for polyester or
          cotton fabric)
 RN
      186910-35-0 HCAPLUS
      1,4-Benzenedicarboxylic acid, dimethyl ester, polymer with
       .alpha.-hydro-.omega.-hydroxypoly(oxy-1,2-ethanediyl),
       .alpha.-methyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl) and
      1,2,3-propanetriol (9CI) (CA INDEX NAME)
      CM
      CRN 25322-68-3
      CMF
            (C2 H4 O)n H2 O
         -сн<sub>2</sub>-сн<sub>2</sub>-о
      CM
            2
      CRN
            9004-74-4
            (C2 H4 O)n C H4 O
      CMF
      CCI
            PMS
          сн<sub>2</sub>-сн<sub>2</sub>-о
      CM
            3
```

CRN 120-61-6 CMF C10 H10 O4

CRN 56-81-5 CMF C3 H8 O3

$$\begin{array}{c} \text{OH} \\ | \\ \text{HO-} \, \text{CH}_2\text{--} \, \text{CH-} \, \text{CH}_2\text{--} \, \text{OH} \end{array}$$

186910-36-1 HCAPLUS

1,4-Benzenedicarboxylic acid, dimethyl ester, polymer with .alpha.-methyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl) and 1,2,3-propanetriol (9CI) (CA INDEX NAME)

CM

CRN 9004-74-4 CMF (C2 H4 O)n C H4 O CCI PMS

CM

CRN 120-61-6 CMF C10 H10 O4

CRN 56-81-5 CMF C3 H8 O3

$$\begin{array}{c} \text{OH} \\ | \\ \text{HO---} \text{CH}_2\text{----} \text{CH} - \text{CH}_2\text{----} \text{OH} \end{array}$$

```
=> d bib abs hitstr 3
     ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2001 ACS
     1996:731922 HCAPLUS
AN
     126:31997
DN
TТ
     Poly(ethylene glycol) Graft Copolymers Containing Carboxylic Acid Groups:
     Aggregation and Viscometric Properties in Aqueous
     Solution
     Derand, Helene; Wesslen, Bengt; Wittgren, Bengt; Wahlund, Karl-Gustav
AU
CS
     Department of Chemical Engineering II, Lund University, Lund, S-221 00,
     Swed.
so
     Macromolecules (1996), 29(27), 8770-8775
     CODEN: MAMOBX; ISSN: 0024-9297
     American Chemical Society
PB
DT
     Journal
LA
     English
     Poly(ethylene glycol) monomethyl ethers (MPEG) were grafted on copolymers
     of maleic anhydride and styrene, Me methacrylate, and ethylhexyl
     methacrylate, resp. Hydrolysis of the remaining anhydride residues gave
     graft copolymers carrying a large no. of carboxylic acid groups along the
     main chains. The properties in aq. solns. of these
     graft copolymers were studied with respect to aggregation behavior and
     viscometric properties. Aggregation of the polymers was examd. by quasi-elastic light scattering and flow field-flow fractionation in water
     and KCl soln. Both methods showed that the anionic graft copolymers
     mainly were present as single mols. in pure water, with a minor fraction
     of aggregates. In KCl soln., aggregates with av. sizes of approx. 30 nm
     were the dominant species. In aq. soln., the polymers exhibited polyelectrolyte behavior, i.e., a dramatic increase of the
     viscosity upon neutralization. Graft copolymers with hydrophobic groups
     in the backbone had lower viscosities.
TT
     53814-38-3
     RL: PRP (Properties)
        (aggregation and viscosity of aq. monomethyl poly(oxyethylene) graft
        copolymers contg. carboxylic acid groups)
RN
     53814-38-3 HCAPLUS
     2,5-Furandione, polymer with ethenylbenzene, ester with
     .alpha.-methyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl), graft (9CI) (CA
     INDEX NAME)
     CM
          1
     CRN 9004-74-4
          (C2 H4 O)n C H4 O
     CMF
     CCI PMS
         сн<sub>2</sub>-сн<sub>2</sub>-
     CM
          2
          9011-13-6
     CMF
           (C8 H8 . C4 H2 O3)x
     CCI
           PMS
           CM
           CRN 108-31-6
```

CMF C4 H2 O3

CM ·

CRN 100-42-5 CMF C8 H8

 $H_2C = CH - Ph$

```
=> d bib abs hitstr 4
     ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2001 ACS
L58
     1992:129953 HCAPLUS
AN
DN
     116:129953
TΙ
     Manufacture of water-soluble ester salts of itaconic acid copolymers
IN
     Wlasiuk, Danuta; Klopotek, Alojzy
PA
     Instytut Chemii Przemyslowej, Pol.
     Pol., 11 pp. Abstracted and indexed from the unexamined application.
     CODEN: POXXA7
DΤ
     Patent
LA
     Polish
FAN.CNT 1
     PATENT NO.
                          KIND DATE
                                                  APPLICATION NO. DATE
                                 19910329
РΤ
                          В1
                                                  PL 1987-265244
                                                                      19870417
     Products useful as complexing agents and surfactants are manufd. by
     partially esterifying 1-10:1-3 itaconic acid-maleic anhydride copolymers
      (I) with 0.01-2.5 mol C10-22 fatty alc., polyethoxylated C10-22 fatty alc. (d.p. 6-20), or polyethoxylated (C6-22-alkyl)phenol at 343-383 K and
     neutralizing with alkali metal hydroxides, NH3, and or alkanolamines at
     293-323 K. Thus, a 130-600 I was heated in dioxane with 6 g
     polyethoxylated nonylphenol (d.p. 8) and stripped to give 245 g product (mol. wt. 5500) which was neutralized (240 g) with 763 g 20% NaOH at 293 K to give a 38.5% soln. of polymer with Ca2+ and Mg2+ complexation 82.9 and
     0.9 mg/g at pH 9 and surface tension of a 0.5% aq. soln
      . 65 dynes/cm.
     139247-10-2P
     RL: PREP (Preparation)
     (manuf. of water sol., for surfactants and complexing agents) 139247-10-2 HCAPLUS
RN
     Butanedioic acid, methylene-, polymer with 2,5-furandione, ester with
      .alpha.-dodecyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl), potassium salt
      (9CI) (CA INDEX NAME)
           1
     CM
           9002-92-0
           (C2 H4 O)n C12 H26 O
     CMF
     CCT
           PMS
                             (CH_2)_{11}-Me
     CM
           2
          28391-42-6
     CRN
     CMF
           (C5 H6 O4 . C4 H2 O3)x
     CCI
           PMS
           CM
           CRN '108-31-6
           CMF C4 H2 O3
```

CM

CRN 97-65-4

CMF C5 H6 O4

$$^{\text{CH}_2}_{||}_{\text{HO}_2\text{C}-\text{C}-\text{CH}_2-\text{CO}_2\text{H}}$$

```
=> d bib abs hitstr 5
L58 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2001 ACS
     1992:42274 HCAPLUS
AN
     116:42274
     Preparation of melt-moldable and water-soluble thermoplastic modified
     maleic anhydride copolymer resins
IN
     Hirashima, Masao; Nozawa, Hiroshi; Kawame, Toshimitsu; Kono, Naotake
     Kuraray Co., Ltd., Japan
     Jpn. Kokai Tokkyo Koho, 9 pp.
     CODEN: JKXXAF
DT
     Patent
LA
     Japanese
FAN.CNT 1
     PATENT NO.
                       KIND DATE
                                             APPLICATION NO.
                                                              DATE
     JP 03163109
                             19910715
                                             JP 1989-283638 19891030
PΤ
                       A2
                             19990412
     JP 2882648
                        В2
PRAI JP 1989-212407
                             19890817
     The title resins giving films with excellent phys. properties are prepd.
     by esterification of maleic anhydride copolymeres with RO(AO)nH I; R =
     C1-10 alkyl; A = (Ph-substituted) C2-4 vicinal alkylene; n .gtoreq.1].
     Thus, after 30.8 g Isobam 04 (wt.-av. mol. wt. 5 .times. 104) was esterified with 17.8 g I (R = Me, A = CH2CH2, n = av. 6) (II) at
     80-90.degree. for 5 h under N with stirring in 100 g DMF in the presence
     of 0.50 g 2-methylimidazole, the DMF and unreacted II were distd. off at
     120.degree. under reduced pressure to obtain 39.5 g a partially esterified
     product (esterification degree 14.9%), which was pressed at 150.degree./50
      kg/cm2(gage) for 3 min to prep. a 1-mm transparent film with softening
     temp. 120.degree. and breaking strength 80 kg/cm2 (gage) and breaking
     extension 30%. The obtained polyester 10, 25% aq. NH3 6.34, and H2O 50 g
     were stirred at 50-60.degree. for 30 min to give a transparent aq
      soln..
.IT
     53814-38-3P 137462-36-3P 138414-49-0P
     138414-52-5P
     RL: PREP (Preparation)
         (prepn. of, thermoplastic and melt-moldable and water-sol, films with
         good phys. properties from)
RN
     53814-38-3 HCAPLUS
     2,5-Furandione, polymer with ethenylbenzene, ester with
      .alpha.-methyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl), graft (9CI) (CA
     INDEX NAME)
     CM
     CRN 9004-74-4
         (C2 H4 O)n C H4 O
     CMF
     CCI PMS
        СН2-СН2-О
     CM
     CRN
          9011-13-6
          (C8 H8 . C4 H2 O3)x
          PMS
     CCI
          CM
                3
           CRN 108-31-6
          CMF C4 H2 O3
```

CM 4

CRN 100-42-5 . CMF C8 H8

 $H_2C = CH - Ph$

RN 137462-36-3 HCAPLUS

CN 2,5-Furandione, polymer with 2-methyl-1-propene, ester with .alpha.-methyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

CM 1

CRN 9004-74-4

CMF (C2 H4 O)n C H4 O

CCI PMS

CM 2

CRN 26426-80-2

CMF (C4 H8 . C4 H2 O3) x

CCI PMS

CM 3

CRN 115-11-7 CMF C4 H8

СH₂ || н₃С-с-сн₃

CM 4

CRN 108-31-6 CMF C4 H2 O3



RN 138414-49-0 HCAPLUS

CN 2,5-Furandione, polymer with ethene, ester with .alpha.-methyl-.omega.hydroxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

CM

CRN 9004-74-4

CMF (C2 H4 O)n C H4 O CCI PMS

CM

CRN 9006-26-2

CMF (C4 H2 O3 . C2 H4)x

CCI PMS

> CM 3

CRN 108-31-6

CMF C4 H2 O3

CM

CRN 74-85-1 CMF C2 H4

$H_2C = CH_2$

138414-52-5 HCAPLUS

2,5-Furandione, polymer with 2-methyl-1-propene, ester with .alpha.-ethyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

CM

CRN 27879-07-8

CMF (C2 H4 O)n C2 H6 O

CCI PMS

$$HO = \begin{bmatrix} CH_2 - CH_2 - O \end{bmatrix}_n$$
 Et

CM

26426-80-2 CRN

CMF (C4 H8 . C4 H2 O3)x

CCI PMS

> CM 3

CRN 115-11-7 CMF C4 H8

CM 4

CRN 108-31-6 CMF C4 H2 O3

display not provided CEPERLEY 09/647,518 for # 4,6-8, => d ti pn 1-28 10-16,23 \$ 25 L74 ANSWER 1 OF 28 USPATFULL Human papillomavirus vaccine formulations TI since they are B1 20010626 PΙ US 6251678 L74 ANSWER 2 OF 28 USPATFULL Treatment of conditions and disease related to a patent PΤ US 6194392 В1 20010227 all ready displayed the kwic format L74 ANSWER 3 OF 28 USPATFULL Cascade polymer complexes, process for their production and ΤI pharmaceutical agents containing said complexes US 6177060 В1 20010123 PI 1.74 ANSWER 4 OF 28 USPATFULL Cascade polymer complexes, process for their production and is provided when pharmaceutical agents containing said complexes ΡI US 6166200 20001226 the abstract is L74 ANSWER 5 OF 28 USPATFULL Use of hyaluronic acid or its derivatives to enhance delivery of ΤI therapeutic agents lacking in hitterms US 6069135 20000530 PΙ WO 9104058 19910404 ANSWER 6 OF 28 USPATFULL L74 Cascade polymer complexes, process for their production and ΤI pharmaceutical agents containing said complexes PΙ 20000516 US 6063361 L74 ANSWER 7 OF 28 USPATFULL Treatment of conditions and disease PΙ

US 6048844 20000411

1.74 ANSWER 8 OF 28 USPATFULL

ΤI Use of hyaluronic acid or its derivatives in peritoneal dialysis and

formulations thereof

PΙ US 5985851 19991116

T.74 ANSWER 9 OF 28 USPATFULL

ΤI Compositions comprising hyaluronic acid and drugs

US 5985850 19991116

ANSWER 10 OF 28 USPATFULL L74

Treatment of conditions and disease TΤ

PΙ US 5932560 19990803

L74 ANSWER 11 OF 28 USPATFULL

Treatment of conditions and disease TΙ

US 5929048 PΙ 19990727

L74 ANSWER 12 OF 28 USPATFULL

ΤI Use of a form of hyaluronic acid and a medicinal agent for reducing

rejection of organs transplantation in mammals $% \left(\mathbf{r}\right) =\mathbf{r}^{\prime }$

РΤ 19990622 US 5914314

ANSWER 13 OF 28 USPATFULL L74

TI Treatment of conditions and disease

PI US 5852002 19981222

T.74 ANSWER 14 OF 28 USPATFULL

Compositions containing a form of hyaluronic acid and a medicinal agent

for treating acne in mammals and methods for administration of such

composition

US 5830882 PΙ 19981103

L74 ANSWER 15 OF 28 USPATFULL

Method of using hyaluronic acid or its pharmaceutically acceptable salts for the treatment of disease

ΡI	US 5827834 19981027				
L74 TI	ANSWER 16 OF 28 USPATFULL Cascade polymer complexes, process for their production and pharamceutical agents containing said complexes				
PI	US 5820849 19981013				
L74 TI	ANSWER 17 OF 28 USPATFULL Method of administering of a hyaluronic acid and an NSAID to decrease side effects of the NSAID				
ΡI	US 5811410 19980922				
L74 TI	ANSWER 18 OF 28 USPATFULL Vaccine composition against influenza, with synergic effects, containing influenza virus core as an additive				
PI	US 5741493 19980421				
L74 TI	ANSWER 19 OF 28 USPATFULL Detergent-facilitated immunoassay for the rapid and quantitative assay of pharmacological agents US 5627080 19970506				
PI					
L74 TI PI	ANSWER 20 OF 28 USPATFULL Contraceptive compositions US 5595980 19970121				
L74 TI	ANSWER 21 OF 28 USPATFULL Process for preparing immunogenic complexes and pharmaceutical composition containing these complexes				
ΡI	US 4900549 19900213				
L74 TI	ANSWER 22 OF 28 USPATFULL Aryl and heteroaryl ethers as agents for the treatment of hypersensitive ailments				
PI	US 4728668 19880301				
L74 TI	ANSWER 23 OF 28 USPATFULL Aryl and heteroaryl ethers as agents for the treatment of hypersensitive ailments				
PI	US 4725619 19880216 .				
L74 TI PI	ANSWER 24 OF 28 USPATFULL Plasminogen activator derivatives US 4640835 19870203				
L74 TI	ANSWER 25 OF 28 USPATFULL Aryl and heteroaryl ethers as agents for the treatment of hypersensitive				
ΡI	ailments US 4631287 19861223				
L74 TI PI	ANSWER 26 OF 28 USPATFULL Composition for diagnostic reagents US 4578282 19860325				
L74 TI PI	ANSWER 27 OF 28 USPATFULL Preservative and fixative preparations for biological systems US 4493821 19850115				
L74 TI PI	ANSWER 28 OF 28 USPATFULL Process for the isolation of membrane proteins from Neisseria meningitidis and vaccines containing same US 4271147 19810602				

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=> d bib abs hitstr 1
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ANSWER 1 OF 28 USPATFULL 2001:97703 USPATFULL AN TI Human papillomavirus vaccine formulations TN Volkin, David B., Doylestown, PA, United States Shi, Li, Eagleville, PA, United States Mach, Henryk, Ambler, PA, United States PΑ Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation) US 6251678 Bl 20010626 PΤ US 2000-496812 20000202 (9) ΑI PRAI US 1999-118723 19990205 (60) DTUtility GRANTED FS EXNAM Primary Examiner: Salimi, Ali R. LREP Giesser, Joanne M., Tribble, Jack L. CLMN Number of Claims: 14 ECL Exemplary Claim: 1 DRWN 6 Drawing Figure(s); 6 Drawing Page(s) LN.CNT 496 CAS INDEXING IS AVAILABLE FOR THIS PATENT. New human papilloma virus (HPV) vaccine formulations exhibit enhanced long-term stability. Formulation components can include: virus-like particles (VLPs) absorbed onto aluminum, a salt, non-ionic $\operatorname{surfactant}$, and a buffer. Additional formulations also contain a polymeric polyanionic stabilizer and a salt either in the presence or absence buffering agents and nonionic detergent. CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 9002-92-0, Brij35 9002-93-1, Triton x-100 **9004-95-9**, Brij 58 (surfactant; human papilloma virus vaccine formulations) RN 9002-92-0 USPATFULL Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA CN INDEX NAME)

$$HO = \begin{bmatrix} -CH_2 - CH_2 - O \end{bmatrix}_n (CH_2)_{11} - Me$$

RN 9002-93-1 USPATFULL CN Poly(oxy-1,2-ethanediy1), .alpha.-[4-(1,1,3,3-tetramethylbuty1)pheny1]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ \text{Me} & & \\ & & & \\ \text{Me} & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

RN 9004-95-9 USPATFULL CN Poly(oxy-1,2-ethanediyl), .alpha.-hexadecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)

HO
$$CH_2-CH_2-O$$
 (CH₂)₁₅-Me

=> d bib abs hitstr 2

L74 ANSWER 2 OF 28 USPATFULL 2001:29544 USPATFULL AN Treatment of conditions and disease ΤI Falk, Rudolf Edgar, Toronto, Canada Asculai, Samuel S., Toronto, Canada IN PΑ Hyal Pharmaceutical Corporation, Mississauga, Canada (non-U.S. corporation) US 6194392 US 1995-460978 PΙ В1 20010227 19950807 (8) AΤ Division of Ser. No. US 1991-675908, filed on 3 Jul 1991 RLI CA 1989-612307 PRAI 19890921 DTUtility FS Granted Primary Examiner: Peselev, Elli EXNAM LREP Hughes, Ivor M., Hughes, Neil H., Sarkis, Marcelo K. Number of Claims: 16 CLMN ECL Exemplary Claim: 1 DRWN 1 Drawing Figure(s); 1 Drawing Page(s) LN.CNT 2517

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A combination for administration to a mammal which combination employs a therapeutically effective amount of a medicinal and/or therapeutic agent to treat a disease or condition and an amount of hyaluronic acid and/or salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **26027-38-3**, Nonoxynol-9

(hyaluronate or salt or deriv. and, for treating herpes, canker sores and shingles, penetration enhancement in relation to)

26027-38-3 USPATFULL RN

Poly(oxy-1,2-ethanediy1), .alpha.-(4-nonylpheny1)-.omega.-hydroxy- (9CI) CN (CA INDEX NAME)

$$\begin{array}{c|c} \text{O-CH}_2\text{-CH}_2 & \text{OH} \\ \text{Me-(CH}_2)_8 & \text{OH} \end{array}$$

=> d kwic 2

L74 ANSWER 2 OF 28 USPATFULL

SUMM . amount of solution given at each administration is generally less than 60 ml, e.g. less than 20 ml, of an aqueous solution of the acid or its salt. It is convenient to administer the acid dissolved in water (<2% w/w, buffered to.

SUMM . of an antiviral agent lacking inhibitory action and a compound (for example, hyaluronic acid) possessing cell fusion inhibitory activity and/or virus-adsorption inhibitory activity for

treating disease carried by a virus. SUMM caused by retroviruses. Hyaluronic acid is taught for prevention or therapy of leukemia or AIDS by suppressing replication of

SUMM An article entitled "Inactivation of Herpes Simplex Viruses by Nonionic Surfactants" by one of the inventors herein (Dr. Samuel Asculai) among others (published in Antimicrobial Agents and Chemotherapy, April 1978, pp.. . . ether or amide linkages between

the hydrophilic and hydrophobic portions of the molecule rapidly inactivated the infectivity of herpes simplex viruses. The activity stemmed from the ability of nonionic surfactants to dissolve lipid-containing membranes. This was confirmed by observing surfactant destruction of mammalian cell plasma membranes and herpes simplex virus envelopes. Proprietary vaginal contraceptive formulations containing nonionic surfactants also inactivated herpes simplex virus infectivity. This observation suggests that nonionic surfactants in appropriate formulation could effectively prevent herpes simplex virus transmission." SUMM . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic surfactants (e.g. cetyl pyridinium chloride) and cationic surfactants (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethanime salt of ketorolac (sold under the. SUMM radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic surfactants (e.g. cetyl pyridium chloride) and cationic surfactants (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. SUMM . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic surfactants (e.g. cetyl pyridinium chloride) and catioinic surfactants (e.g. benzalkonium chloride), non-steroidal
anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. SUMM radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic surfactants (e.g. cetyl pyridium chloride) and cationic surfactants (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. SUMM . or condition (for example ascorbic acid (Vitamin C)), Vitamin ${\tt C}$ (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic surfactant, e.g. nonoxynol-9 (nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic surfactants (e.g. cetyl pyridinium chloride) and cationic surfactants (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. SUMM radical scavenger (for example ascorbic acid (Vitamin C), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic surfactants (e.g. cetyl pyridinium chloride) and cationic surfactants (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. SUMM . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic

```
surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . .
SUMM
                 either intravenously, intra-arterially, intraperitoneally or
       intrapleurally or directly into the tumor by injection through a needle
       placed under sonographic or CT guidance.
       According to another aspect of the invention, the combination of a non-ionic surfactant for example nonoxynol-9 [nonylphenoxy
SUMM
       polyethoxy ethanol] [found in Delfen (t.m.) contraceptive cream] and
       hyaluronic acid and/or salts thereof and other.
       The non-ionic surfactant preferably comprises an ether or an
       amide linkage between the hydrophilic and hydrophobic portions of the
       molecule, being more active than the surfactants having an
       ester- or an ether- ester linkage.
       The following nonionic surfactants and identified linkages are
SUMM
       offered for consideration.
SUMM
        Surfactant
None (control virus)
5% Nonoxynol-9 (nonylphenoxy-polyethoxy ethanol) Ether
1% Triton X-100 (p-diisobutylphenoxy-polyethoxy Ether
  -ethanol)
1% Brij-97 (polyoxyethylene (10) oleyl ether) Ether
1% Span-20 (sorbitran monclamate)
                                                Ester
1% Span-80.
SUMM
       (h) non-antigenic."
           . . person suffering brain trauma
SUMM
                                 minoxidil - combination -
2.
       Hair growth
                                 grow more hair when applied
                                 topically
3.
       Herpes, canker sore,
                                 nonionic surfactants, e.g.,
                                 nonoxynol-9 and
       shingles
                                 anionic, (e.g. cetyl
                                 pyridinium chloride) and
                                 cationic (e.g.
                                 benzalkonium choride),
                                   surfactants
       Renal failure, cardiac diuretics - furosemide insufficiency, hypertension,
4.
       edema
5.
       Infection, acne,
                                 antibiotics, antibacterials,
       mononucleosis
                                 antimicrobials, etc.,
                                 ascorbic
                                 acid and hyaluronic.
DETD
       On sequential CT scan this patient shows significant
       improvement in size of the residual mass. As soft tissue sarcomas are so
       verv resistant.
       Patient was given CT Scan of the abdomen and pelvis. There is
DETD
       moderate hepatic steatosis without evidence of metastatic disease. The
       spleen, pancreas, adrenals.
                treatment, the patient has made good improvement. She has
DETD
       gained weight, and is no longer feeling any pain. The carcinoembryonic
       antigen is down to 26 nonograms/ml and steadily falling.
DETD
              . and an MRI scan was undertaken to try and demonstrate this. It
       showed somewhat abnormalities in the appropriate area. A CT
       scan of the region was unhelpful.
DETD
       This man has a mesothelioma following surgical resection and then
       adjuvant treatment. It is now seven years since the initial
       diagnosis. In the spring of this year he developed a recurrence.
DETD
                biopsy, but apparently there was regrowth and worsening of the
       pain with partial ureteric obstruction demonstrated as shown by a
       CT scan of the abdomen and pelvis done Jun. 28, 1990.
IT 26027-38-3, Nonoxynol-9
         (hyaluronate or salt or deriv. and, for treating herpes, canker sores
        and shingles, penetration enhancement in relation to)
```

=> d bib abs hitstr 3 L74 ANSWER 3 OF 28 USPATFULL 2001:10522 USPATFULL ΑN Cascade polymer complexes, process for their production and TΙ pharmaceutical agents containing said complexes IN Schmitt-Willich, Heribert, Berlin, Germany, Federal Republic of Platzek, Johannes, Berlin, Germany, Federal Republic of Raduchel, Bernd, Berlin, Germany, Federal Republic of Muhler, Andreas, Neuenhagen, Germany, Federal Republic of Frenzel, Thomas, Berlin, Germany, Federal Republic of Schering Aktiengeseuschaft, Berlin, Germany, Federal Republic of PA (non-U.S. corporation) US 6177060 ΡI В1 20010123 US 1998-44254 19980319 (9) AΙ Division of Ser. No. US 1996-674844, filed on 3 Jul 1996, now patented, RLI Pat. No. US 5820849 PRAI DE 1995-19525924 19950704 DΤ Utility FS Granted EXNAM Primary Examiner: Hartley, Michael G. LREP Millen, White, Zelano & Branigan, P.C. CLMN Number of Claims: 8 Exemplary Claim: 1 ECL 1 Drawing Figure(s); 1 Drawing Page(s) DRWN LN.CNT 1880 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Cascade polymer complexes with at least 16 ions of an element of atomic numbers 20 to 29, 39, 42, 44 or 57-83, useful NMR or x-ray lymphography imaging. CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 23601-40-3, Hexaethylene glycol monomethyl ether (prepn. of cascade polymer complexes as medical contrast media) 23601-40-3 USPATFULL

PAGE 1-A

MeO-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-

2,5,8,11,14,17-Hexaoxanonadecan-19-ol (8CI, 9CI) (CA INDEX NAME)

PAGE 1-B

--- cн₂-- сн₂-- он

RN

CN

=> d bib abs hitstr 5

L74 ANSWER 5 OF 28 USPATFULL 2000:67724 USPATFULL AN Use of hyaluronic acid or its derivatives to enhance delivery of ΤI therapeutic agents Falk, Rudolf Edgar, Toronto, Canada Asculai, Samuel S., Toronto, Canada TN Hyal Pharmaceutical Corporation, Mississauga, Canada (non-U.S. PA corporation) US 6069135 20000530 PΤ WO 9104058 19910404 US 1991-675908 19910703 (7) WO 1990-CA306 19900918 19910703 PCT 371 date 19910703 PCT 102(e) date PRAI CA 1989-612307 19890921 Utility DT FS Granted EXNAM Primary Examiner: Fonda, Kathleen K. Hughes, Ivor M., Hughes, Neil H., Sarkis, Marcelo K. LREP CLMN Number of Claims: 139 ECL Exemplary Claim: 1 1 Drawing Figure(s); 1 Drawing Page(s) DRWN LN.CNT 2830 CAS INDEXING IS AVAILABLE FOR THIS PATENT. AB A pharmaceutical composition is provided comprising:

- (1) an agent selected from a medicinal agent and a therapeutic agent and combinations thereof in a therapeutically effective amount to treat a disease or condition in humans who will benefit from the treatment with the agent; and
- (2) hyaluronic acid and/or pharmaceutically acceptable salts thereof and/or fragments, and subunits of hyaluronic acid, characterized in that said composition
- (a) is in a dosage form which is suitable for administration in humans;
- (b) is in a form in which (i) component (1) is in an effective dosage amount to treat said disease or condition by penetration at the site to be treated; and (ii) component (2) is immediately available to transport component (1) at the site to be treated, and which component (2) is in an effective non-toxic amount to facilitate the transport of component (1) upon administration, through the tissue including scar tissue, at the site to be treated and through the cell membranes or the individual cells to be treated, wherein said amount of component (2) is sufficient to provide a dosage greater than 10 mg/70 kg person of component (2).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 26027-38-3, Nonoxynol-9

(hyaluronate or salt or deriv. and, for treating herpes, canker sores and shingles, penetration enhancement in relation to)

26027-38-3 USPATFULL Poly(oxy-1,2-ethanediy1), .alpha.-(4-nonylphenyl)-.omega.-hydroxy- (9CI) CN (CA INDEX NAME)

$$O-CH_2-CH_2$$
 OH

Me-(CH₂)8

=> d kwic 5

```
L74 ANSWER 5 OF 28 USPATFULL
         . . amount of solution given at each administration is generally
       less than 60 ml, e.g. less that 20 ml, of an aqueous
       solution of the acid or its salt. It is convenient to administer
       the acid dissolved in water (<2% w/w, buffered to.
SUMM
            . of an antiviral agent lacking inhibitory action and a compound
       [for example, hyaluronic acid] possessing cell fusion inhibitory
       activity and/or virus-adsorption inhibitory activity for
       treating disease carried by a virus.
            . action, being perhaps anesthetics, analgesics, anti
SUMM
       inflammatories, wound healers, antimicrobics, adrenergic agonsits and
       antagonists, cytostatics, antirheumatics, antihypertensives, diuretics,
       sexual hormones, immunostimulants and immunosuppressants, for example, one of the drugs having the activity already described for the
       therapeutically active alcohols to be.
SUMM
            . caused by retroviruses. Hyaluronic acid is taught for
       prevention or therapy of leukemia or AIDS by suppressing replication of
       the virus.
SUMM
       An article entitled "Inactivation of Herpes Simplex Viruses by
       Nonionic Surfactants" by one of the inventors herein (Dr.
       Samuel Asculai) among others [published in Antimicrobial Agents and
       Chemotherapy, April 1978, pp.686-690]. . . ether or amide linkages
       between the hydrophilic and hydrophobic portions of the molecule rapidly
       inactivated the infectivity of herpes simplex viruses. The
       activity stemmed from the ability of nonionic surfactants to
       dissolve lipid-containing membranes. This was confirmed by observing
       surfactant destruction of mammalian cell plasma membranes and
       herpes simplex virus envelopes. Proprietary vaginal
       contraceptive formulations containing nonionic surfactants
       also inactivated herpes simplex virus infectivity. This
       observation suggests that nonionic surfactants in appropriate
       formulation could effectively prevent herpes simplex virus
       transmission."
DETD
               radical scavenger (for example ascorbic acid (Vitamin C)),
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy
       ethanol] found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (.+-.) tromethamine salt of ketorolac (sold under the.
               radical scavenger (for example ascorbic acid (Vitamin C)),
DETD
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy
       ethanol] found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (.+-.) tromethamine salt of ketorolac (sold under the.
               radical scavenger (for example ascorbic acid (Vitamin C)),
DETD
       vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 (nonylphenoxy polyethoxy
       ethanol] found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (.+-.) tromethamine salt of ketorolac (sold under the.
                radical scavenger (for example ascorbic acid (Vitamin C)),
DETD
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy
       ethanol) found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
```

```
anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (.+-.) tromethamine salt of ketorolac (sold under the.
DETD
          . . radical scavenger (for example ascorbic acid (Vitamin C)),
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 (nonylphenoxy polyethoxy
       ethanol] found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (.+-.) tromethamine salt of ketorolac (sold under the.
                 radical scavenger (for example ascorbic acid (Vitamin C)),
DETD
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy
       ethanol] found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (.+-.) tromethamine salt of ketorolac (sold under the.
DETD
                radical scavenger (for example ascorbic acid (Vitamin C)),
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy
       ethanol) found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (.+-.) tromethamine salt of ketorolac (sold under the.
DETD
                either intravenously, intra-arterially, intraperitoneally or
       intrapleurally or directly into the tumor by injection through a needle
       placed under sonographic or CT guidance.
According to another aspect of the invention, the combination of a non-ionic surfactant for example nonoxynol-9 [nonylphenoxy
DETD
       polyethoxy ethanol] [found in Delfen (t.m.) contraceptive cream] and
       hyaluronic acid and/or salts thereof and other.
DETD
       The non-ionic surfactant preferably comprises an ether or an
       amide linkage between the hydrophilic and hydrophobic portions of the
       molecule, being more active than the surfactants having an
       ester--or an ether--ester linkage.
       The following nonionic surfactants and identified linkages are
       offered for consideration.
DETD
  Surfactant
                                Linkage
None (control virus)
5% Nonoxynol-9 (nonylphenoxy-polyethoxy ethanol)
                              Ether
1% Triton X-100 (p-diisobutylphenoxy-polyethoxy
                              Ether
```

```
1% Brij-97 (polyoxyethylene (10) oleyl ether)
                            Ether
1% Span-20 (sorbitran monclamate)
                            Ester
1% Span-80 (sorbitan.
     (h) non-antigenic."
DETD
DETD
             . person suffering brain trauma
                            minoxidil - combination -
2.
          Hair growth
                             grow more hair when applied
                             topically
3.
          Herpes, canker sore,
                            nonionic surfactants, e.g.,
                            nonoxynol-9 and
          shingles
                             anionic, (e.g. cetyl
                             pyridinium chloride) and
                             cationic (e.g.
                             benzalkonium choride),
                              surfactants
4.
          Renal failure, cardiac
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diuretics - furosemide

insufficiency, hypertension,

edema

5.

Infection, acne, antibiotics, antibacterials, mononucleosis antimicrobials, etc., ascorbic

acid and hyaluronic.

- DETD On sequential **CT** scan this patient shows significant improvement in size of the residual mass. As soft tissue sarcomas are so very resistant. . .
- DETD Patient was given CT Scan of the abdomen and pelvis. There is moderate hepatic steatosis without evidence of metastatic disease. The spleen, pancreas, adrenals. . .
- DETD . . . treatment, the patient has made good improvement. She has gained weight, and is no longer feeling any pain. The carcinoembryonic antigen is down to 26 nonograms/ml and steadily falling.
- DETD . . . and an MRI scan was undertaken to try and demonstrate this. It showed somewhat abnormalities in the appropriate area. A CT scan of the region was unhelpful.
- DETD This man has a mesothelioma following surgical resection and then adjuvant treatment. It is now seven years since the initial diagnosis. In the spring of this year he developed a recurrence.
- DETD . . . biopsy, but apparently there was regrowth and worsening of the pain with partial ureteric obstruction demonstrated as shown by a CT scan of the abdomen and pelvis done Jun. 28, 1990.

CLM What is claimed is:

- . the agent is selected from the group consisting of free radical scavengers, ascorbic acid (Vitamin C), anti-cancer drugs, chemotherapeutic drugs, anti-viral drugs, non-steroidal anti-inflammatory drugs (NSAID), steroidal anti-inflammatory drugs, anti-fungal drugs, detoxifying drugs, analgesics, bronchodilators, anti-bacterial drugs, antibiotic drugs for treatment. . . 6. The method of claim 1 or 2 wherein the agent is an anti-viral drug.
- 21. The method of claim 1 or 2 wherein the agent is a non-ionic surfactant drug.
- 26. The method of claim 21 wherein the non-ionic $\operatorname{surfactant}$ is nonoxynol-9.
- 27. The method of claim 21 wherein the non-ionic surfactant further comprises an ether or an amide linkage between the hydrophilic and hydrophobic portions of the surfactant.
- 32. The method of claim 1 or 2 wherein the disease or condition is selected from the group consisting of a neoplastic condition, acne, AIDS, Berger's disease, a condition requiring bronchodilation, canker sore, chronic bacterial infection, fungal infection, diabetes, viral disease, epitheloid sarcoma, herpes, shingles, hypertension, infection, inflammation, malfunctioning kidney, renal failure, kyphosis, leomyosarcoma, leukemia, mesothelioma, metastatic disease, mononucleosis, pain, . .
- . of claim 1 or 2 wherein the disease or condition is a canker sore and wherein the agent is a surfactant selected from the group consisting of non-ionic surfactants, ionic surfactants and cationic surfactants.
- 41. The method of claim 40 wherein the **surfactant** is selected from the group consisting of nonoxynol-9, cetyl pyridinium chloride and benzalkonium chloride.
- 45. The method of claim 1 or 2 wherein the disease or condition is ${\bf viral}$ disease.
- . The method of claim 1 or 2 wherein the disease or condition is herpes and wherein the agent is a **surfactant** selected from the group consisting of nonoxynol-9, cetyl pyridinium chloride and benzalkonium chloride.

- . The method of claim 1 or 2 wherein the disease or condition is shingles and wherein the agent is a **surfactant** selected from the group consisting of nonoxynol-9, cetyl pyridinium chloride and benzalkonium chloride.
- . the agent is selected from the group consisting of free radical scavengers, ascorbic acid (Vitamin C), anti-cancer drugs, chemotherapeutic drugs, anti-viral drugs, non-steroidal anti-inflammatory drugs (NSAID), steroidal anti-inflammatory drugs, anti-fungal drugs, detoxifying drugs, analgesics, bronchodilators, anti-bacterial drugs, antibiotic drugs for treatment. . . 71. The method of claim 66 or 67 wherein the agent is an anti-viral drug.
- 86. The method of claim 66 or 67 wherein the agent is a non-ionic surfactant drug.
- 91. The method of claim 86 wherein the non-ionic $\operatorname{surfactant}$ is nonoxynol-9.
- 92. The method of claim 86 wherein the non-ionic surfactant further comprises an ether or an amide linkage between the hydrophilic and hydrophobic portions of the surfactant.
- 97. The method of claim 66 or 67 wherein the disease or condition is selected from the group consisting of a neoplastic condition, acne, AIDS, Berger's disease, a condition requiring bronchodilation, canker sore, chronic bacterial infection, fungal infection, diabetes, viral disease, epitheloid sarcoma, herpes, shingles, hypertension, infection, inflammation, malfunctioning kidney, renal failure, kyphosis, leomyosarcoma, leukemia, mesothelioma, metastatic disease, mononucleosis, pain, . .
- . of claim 66 or 67 wherein the disease or condition is a canker sore and wherein the agent is a surfactant selected from the group consisting of non-ionic surfactants, ionic surfactants and cationic surfactants.
- 106. The method of claim 105 wherein the **surfactant** is selected from the group consisting of nonoxynol-9, cetyl pyridinium chloride and benzalkonium chloride.
- 110. The method of claim 66 or 67 wherein the disease or condition is $\ensuremath{\text{\textbf{viral}}}$ disease.
- . The method of claim 66 or 67 wherein the disease or condition is herpes and wherein the agent is a **surfactant** selected from the group consisting of nonoxynol-9, cetyl pyridinium chloride and benzalkonium chloride.
- . The method of claim 66 or 67 wherein the disease or condition is shingles and wherein the agent is a surfactant selected from the group consisting of nonoxynol-9, cetyl pyridinium chloride and benzalkonium chloride.
- - (hyaluronate or salt or deriv. and, for treating herpes, canker sores and shingles, penetration enhancement in relation to)

=> d bib abs hitstr 9

L74 ANSWER 9 OF 28 USPATFULL AN 1999:146549 USPATFULL TI Compositions comprising hyaluronic acid and drugs Falk, Rudolf Edgar, Toronto, Canada Asculai, Samuel S., Toronto, Canada IN PA Hyal Pharmaceuticals Corporation, Mississauga, Canada (non-U.S. corporation) US 5985850 US 1995-462154 ΡI 19991116 19950605 (8) AΙ Division of Ser. No. US 675908 RLT PRAI CA 1989-612307 19890921 DTUtility FS Granted EXNAM Primary Examiner: Peselev, Elli LREP Hughes, Ivor M., Hughes, Neil H., Sarkis, Marcelo K. CLMN Number of Claims: 92 ECL Exemplary Claim: 1 DRWN 1 Drawing Figure(s); 1 Drawing Page(s) LN.CNT 2760 CAS INDEXING IS AVAILABLE FOR THIS PATENT. A dosage amount of a pharmaceutical composition comprising a therapeutically effective amount of an agent to treat a disease or condition involving underperfused tissue and pathological tissue in humans and a form of hyaluronic acid, wherein the form of hyaluronic acid is available to transport the agent from the point of administration to the site to be treated. CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 26027-38-3, Nonoxynol-9 (hyaluronate or salt or deriv. and, for treating herpes, canker sores and shingles, penetration enhancement in relation to) RN 26027-38-3 USPATFULL ${\tt Poly(oxy-1,2-ethanediyl),\ alpha.-(4-nonylphenyl)-.omega.-hydroxy-\ (9CI)}$ CN (CA INDEX NAME)

$$O-CH_2-CH_2$$
 OH

Me-(CH₂) 8

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=> d bib abs hitstr 17
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ANSWER 17 OF 28 USPATFULL 1998:115725 USPATFULL AN Method of administering of a hyaluronic acid and an NSAID to decrease TΙ side effects of the NSAID Falk, Rudolf Edgar, Toronto, Canada Asculai, Samuel S., Toronto, Canada Hyal Pharmaceutical Corporation, Mississauga, Canada (non-U.S. TN PA corporation) PΤ 19980922 US 5811410 US 4653351 19950605 (8) AΙ 675908, filed on 3 Jul 1991 RLI Division of Ser. No. PRAI CA 612307 19890921 DT Utility FS Granted EXNAM Primary Examiner: Fonda, Kathleen K. Hughes, Ivor M., Hughes, Neil H., Sarkis, Marcelo K. LREP Number of Claims: 7 CLMN Exemplary Claim: 1 ECL DRWN 1 Drawing Figure(s); 1 Drawing Page(s) LN.CNT 2340 CAS INDEXING IS AVAILABLE FOR THIS PATENT. A method of administering a medicinal agent and an effective amount of a AB form of hyaluronic acid for decreasing side effects associated with using the agent alone in treating a disease or condition in mammals is disclosed. The agent may be a non-steroidal anti-inflammatory drug (NSAID). The amount of hyaluronic acid is sufficient enough to provide a dosage greater than 200 mg/70 kg person. The molecular weight of the form of hyaluronic acid may be less than 750,000 daltons. CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 26027-38-3, Nonoxynol-9

(hyaluronate or salt or deriv. and, for treating herpes, canker sores

26027-38-3 USPATFULL Poly(oxy-1,2-ethanediyl), .alpha.-(4-nonylphenyl)-.omega.-hydroxy- (9CI)

and shingles, penetration enhancement in relation to)

_ о- сн₂- сн₂-

(CA INDEX NAME)

RN

Me- (CH2) 8

=> d kwic 17

L74 ANSWER 17 OF 28 USPATFULL

SUMM . amount of solution given at each administration is generally less than 60 ml, e.g. less that 20 ml, of an aqueous solution of the acid or its salt. It is convenient to administer the acid dissolved in water (<2% w/w, buffered to.

SUMM . of an antiviral agent lacking inhibitory action and a compound [for example, hyaluronic acid] possessing cell fusion inhibitory activity and/or virus-adsorption inhibitory activity for treating disease carried by a virus.

. . . action, being perhaps anesthetics, analgesics, anti inflammatories, wound healers, antimicrobics, adrenergic agonsits and SUMM antagonists, cytostatics, antirheumatics, antihypertensives, diuretics, sexual hormones, immunostimulants and immunosuppressants, for example, one of the drugs having the activity already described for the

SUMM

```
prevention or therapy of leukemia or AIDS by suppressing replication of
       the virus.
       An article entitled "Inactivation of Herpes Simplex Viruses by Nonionic Surfactants" by one of the inventors herein (Dr.
SUMM
       Samuel Asculai) among others [published in Antimicrobial Acrents and
       Chemotherapy, April 1978, pp. 686-690]. . . ether or amide linkages between the hydrophilic and hydrophobic portions of the molecule rapidly
       inactivated the infectivity of herpes simplex viruses. The
       activity stemmed from the ability of nonionic surfactants to
       dissolve lipid-containing membranes. This was confirmed by observing
       surfactant destruction of mammalian cell plasma membranes and
       herpes simplex virus envelopes. Proprietary vaginal
       contraceptive formulations containing nonionic surfactants
       also inactivated herpes simplex virus infectivity. This
       observation suggests that nonionic surfactants in appropriate
       formulation could effectively prevent herpes simplex virus
       transmission."
SUMM
             . radical scavenger (for example ascorbic acid (Vitamin C))),
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy
       ethanol) found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (+/-) tromethamine salt of ketorolac (sold under the.
SUMM
                radical scavenger (for example ascorbic acid (Vitamin C)),
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy
       ethanol] found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (+/-) tromethamine salt of ketorolac (sold under the.
SUMM
                radical scavenger (for example ascorbic acid (Vitamin C)),
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy
       ethanol) found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (+/-) tromethamine salt of ketorolac (sold under the.
               radical scavenger (for example ascorbic acid (Vitamin C)),
SUMM
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy
       ethanol) found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (+/-) tromethamine salt of ketorolac (sold under the.
SUMM
                radical scavenger (for example ascorbic acid (Vitamin C)),
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 (nonylphenoxy polyethoxy
       ethanol] found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (+/-) tromethamine salt of ketorolac (sold under the.
             . radical scavenger (for example ascorbic acid (Vitamin C)),
SUMM
       Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
       chemotherapeutic agent, anti-viral agents for example a
       nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy
       ethanol] found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
       surfactants (e.g. benzalkonium chloride), non-steroidal
       anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
```

```
(+/-) tromethamine salt of ketorolac (sold under the.
             . radical scavenger (for example ascorbic acid (Vitamin C)),
SUMM
      Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,
      chemotherapeutic agent, anti-viral agents for example a
      nonionic surfactant, e.g. nonoxynol-9 [nonylphenoxy polyethoxy
      ethanol] found in Delfen.TM. contraceptive cream, and anionic
       surfactants (e.g. cetyl pyridinium chloride) and cationic
      surfactants (e.g. benzalkonium chloride), non-steroidal
      anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and
       (+/-) tromethamine salt of ketorolac (sold under the.
                either intravenously, intra-arterially, intraperitoneally or
SUMM
      intrapleurally or directly into the tumor by injection through a needle
      placed under sonographic or CT guidance.
      According to another aspect of the invention, the combination of a
SUMM
      non-ionic surfactant for example nonoxynol-9 [nonylphenoxy
      polyethoxy ethanol] [found in Delfen (t.m.) contraceptive cream] and
      hyaluronic acid and/or salts thereof and other.
SUMM
      The non-ionic surfactant preferably comprises an ether or an
      amide linkage between the hydrophilic and hydrophobic portions of the
      molecule, being more active than the surfactants having an
      ester- or an ether-ester linkage.
SUMM
      The following nonionic surfactants and identified linkages are
      offered for consideration.
SUMM
                              Linkage
 Surfactant
None (control virus)
5% Nonoxynol-9 (nonylphenoxy-polyethoxy ethanol)
                            Ether
1% Triton X-100 (p-diisobutylphenoxy-polyethoxy-
                            Ether
ethanol)
1% Brij-97 (polyoxyethylene (10) oleyl ether)
                            Ether
1% Span-20 (sorbitran monclamate)
                            Ester
1% Span-80 (sorbitan.
SUMM (h) non-antigenic."
SUMM
         . . person suffering brain trauma
                      minoxidil - combination -
    Hair growth
                       grow more hair when applied
                       topically
    Herpes, canker sore,
                       nonionic surfactants, e.g.,
                       nonoxynol-9 and
    shingles
                       anionic, (e.g. cetyl
                       pyridinium chloride) and
                       cationic (e.g.
                       benzalkonium choride),
                         surfactants
    Renal failure, cardiac
                       diuretics - furosemide
    insufficiency, hypertension,
    edema
5.
    Infection, acne,
                      antibiotics, antibacterials,
    mononucleosis
                       antimicrobials, etc.,
                       ascorbic
                       acid and hyaluronic.
DETD
      On sequential CT scan this patient shows significant
      improvement in size of the residual mass. As soft tissue sarcomas are so
      verv resistant.
      Patient was given CT Scan of the abdomen and pelvis. There is
DETD
      moderate hepatic steatosis without evidence of metastatic disease. The
      spleen, pancreas, adrenals.
               treatment, the patient has made good improvement. She has
DETD
      gained weight, and is no longer feeling any pain. The carcinoembryonic
      antigen is down to 26 nonograms/ml and steadily falling.
DETD
            . and an MRI scan was undertaken to try and demonstrate this. It
       showed somewhat abnormalities in the appropriate area. A CT
```

scan of the region was unhelpful.

- DETD This man has a mesothelioma following surgical resection and then adjuvant treatment. It is now seven years since the initial diagnosis. In the spring of this year he developed a recurrence. . .

 DETD . . . biopsy, but apparently there was regrowth and worsening of the pain with partial ureteric obstruction demonstrated as shown by a CT scan of the abdomen and pelvis done Jun. 28, 1990.

 IT 26027-38-3, Nonoxynol-9

 (hyaluronate or salt or derive and for treating bernes carbon sorts)
- (hyaluronate or salt or deriv. and, for treating herpes, canker sores and shingles, penetration enhancement in relation to)

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=> d bib abs hitstr 18
   ANSWER 18 OF 28 USPATFULL
       1998:42069 USPATFULL
AN
       Vaccine composition against influenza, with synergic effects,
TТ
       containing influenza virus core as an additive
IN
       Moste-Deshairs, Catherine, Ecully, France
       Meignier, Bernard, Thurins, France
       Pasteur Merieux Serums et Vaccins, Lyons, France (non-U.S. corporation)
PA
       US 5741493
                               19980421
PΙ
ΑI
       US 1995-375224
                               19950119 (8)
       Continuation of Ser. No. US 1992-927261, filed on 22 Nov 1992, now
RLI
       abandoned
PRAI
       FR 1991-806
                           19910124
DT
       Utility
FS
       Granted
EXNAM Primary Examiner: Minnifield, N. M.
LREP
       Curtis Morris & Safford P.C.
      Number of Claims: 56
CLMN
       Exemplary Claim: 1
ECL
DRWN
       7 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 946
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The use, when preparing a vaccine composition containing a
       standard influenza virus vaccine, of an additive
       which consists of a core or core fraction of at least one influenza
       virus, especially a fraction containing protein M; and a
       vaccine composition thereby obtained. The use of said additive
       improves the vaccine's effectiveness.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 9002-92-0
        (in M protein sepn. for influenza vaccine component)
RN
     9002-92-0 USPATFULL
     Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA
CN
       INDEX NAME)
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HO
$$-CH_2-CH_2-O$$
 CH_2 $11-Me$

=> d kwic 18

L74 ANSWER 18 OF 28 USPATFULL Vaccine composition against influenza, with synergic effects, containing influenza virus core as an additive AB The use, when preparing a vaccine composition containing a standard influenza virus vaccine, of an additive which consists of a core or core fraction of at least one influenza virus, especially a fraction containing protein M; and a vaccine composition thereby obtained. The use of said additive improves the vaccine's effectiveness. The object of the present invention is a vaccine composition against influenza, with synergic effects, containing influenza virus core, or a fraction thereof, as an additive to the influenza vaccine. SUMM The influenza virus comprises a lipoprotein envelope surrounding a nucleoprotein "core". The envelope more particularly includes two glycoproteins, hemagglutinin (HA) and neuraminidase (NA). The core is a complex arrangement of viral ribonucleic acid and of several so-called "internal" proteins (polymerases, membrane protein (M) and nucleoprotein (NP)) At present it is known that the influenza vaccine, even when correctly applied, does not completely protect all the subjects

vaccinated: see for example Murphy & Webster, in `Virology, 2ns

edition (Fields et al. Ed.) 1091-1152 (1990), in particular p. 1128. It was therefore desirable to improve the existing vaccines. SUMM SUMM The influenza vaccines currently used are inactivated vaccines: they may be constituted of entire virions, or of virions subjected to treatment with agents which dissolve lipids ("split" vaccines), or else of purified glycoproteins ("sub-unit vaccines"). These inactivated vaccines mainly protect by causing synthesis of the receiver's antibodies directed against the hemagglutinin. It is known that antigenic evolution of the influenza virus by mutation results basically in modifications in HA and NA, while the internal proteins are only slightly modified. The result is that inactivated vaccines used at present only protect effectively as regards the strains the surface glycoproteins of which are identical or antigenically very close to those of the vaccine strains. To obtain a sufficient antigenic spectrum, the vaccines are obtained from several viral strains; they generally contain two type A strains and one type B strain. To adapt the composition of the vaccines to the antigenic evelution of the influenza viruses, the choice of strains for use in the vaccines is reviewed annually depending on the WHO or the American Food and Drug Administration recommendations, these recommendations being based on the results of international epidemiological observations. It is known that the recommended viral strains may be obtained notably from the the following organisations: SUMM It has now been discovered that it is possible to obtain a vaccine composition with synergic effect by associating influenza virus core, or an active fraction of core, with the conventional influenza vaccine. SUMM An active core fraction is one which, when used as an additive to a conventional vaccine, improves the effect of the SUMM Moreover, a protection against virus subtypes not used in the preparation of the components of the vaccine (conventional and added core or core fraction) may be obtained. SUMM The object of the present invention, then, is a vaccine composition against influenza containing the constituents of a conventional influenza vaccine, and further containing core of at least one influenza virus strain, or a fraction of the said core, as an additive. SUMM The conventional vaccine forming the main constituent of the vaccine composition of the invention may be an anti-influenza vaccine with complete virions, a sub-unit vaccine or a split vaccine. It may be obtained from viruses cultivated in chick embryonated eggs, or on cells. SUMM The conventional vaccines may be prepared according to known methods, which are described by Murphy & Wzbster, op. cit., for example. Other details. Complete Virion Vaccine: this may be prepared as follows: the SUMM influenza virus, obtained by culture on chick embryonated eggs, or by culture on cells, is concentrated by ultrafiltration and then purified by. Subunit Vaccine: such a vaccine may be prepared as SUMM follows: using viral suspensions fragmented by treatment with detergent, the surface antigens (hemagglutinin, neuraminidase) are purified, by ultracentrifugation for example. The sub-unit vaccines thus contain mainly HA protein, and possible NA. The detergent used by be cationic detergent for SUMM example, such as hexadecyl trimethyl ammonium bromide (Bachmeyer, Intervirology, 5, 260-272 (1975)), an anionic detergent such as ammonium deoxycholate (Laver & Webster, Virology 69, 511-522, 1976; Webster et al., The Journal of Immunology, Vol. 119, 2073-2077, 1977); or a nonionic detergent such as that commercialized under the name TRITON X100. SUMM Split Vaccine: It can be prepared as follows: an aqueous suspension of the purified virus obtained as above,

inactivated or not, is treated, under stirring, by lipid solvents such

as ethyl ether or chloroform, associated with detergents. The

dissolution of the **viral** envelope lipids results in fragmentation of the **viral** particles. The aqueous phase is recuperated containing the split vaccine, constituted mainly of hemagglutinin and neuraminidase with their original lipid environment removed, and the core or its degradation products. Then. Conventional vaccines generally contain 10 to 15 .mu.g of hemagglutinin from each of the strains entering into their composition. SUMM SUMM The conventional influenza vaccine forming the main constituent of the vaccine composition of the invention may originate from a virus of type A, B or C, or from at least two of these three types. The same applies to the. SUMM The core or fraction of core may be prepared from viruses from the same strain as the main constituent of the composition, or from a different strain or strains, which may. The nomenclature of the influenza viruses and their SUMM classification into types and sub-types are described for example in WHO Bull. 58, 585-591 (1980), and in Murphy & Webster, op. cit. It is known, in particular, that human influenza virus type A includes H1N1, H2N2 and H3N2 subtypes. SUMM In the composition of the invention, the first and second constituents, that is the conventional vaccine and the additive, may be put together in the same container. They may also be present in separate containers placed. The two constituents of the vaccine composition of the invention, whether together or separate, may also be presented in freeze-dried form. The liquid composition is then. . . The composition of the invention is generally presented in the form of SUMM individual vaccine doses (unit doses), constituted either by a vaccinating-unit dose of the two constituents mixed, or by a unit dose of conventional vaccine and a unit dose of core or fraction of core. of the composition of the invention (core) may be obtained SUMM according to known methods, particularly by treatment of the influenza virus using a protease such as bromelain. This treatment allows the envelope proteins to be separated from the core particles; see. SUMM The second constituent of the vaccine composition of the invention may also be composed of an active fraction of influenza virus core, this fraction being a protein or lipoprotein fraction, containing at least one active core protein (particularly M . fraction", designate a protein or fragment of protein), or. protein or core fraction capable of participating in the protection induced by the vaccine, like the core particles themselves. The active fragments may be determined by simple routine experiments, retaining those fragments which, associated with the first constituent of the vaccine composition, give better protection than that obtained with the first constituent (conventional vaccine) alone. SUMM The core fractions, including a core protein or the fragments of the said protein, may be prepared either by virus culture and extraction, or by genetic engineering methods, or by peptidic synthesis, according to methods known per se. it should. SUMM The second constituent (additive) of the vaccine of the invention is particularly M protein, or membrane protein, sometimes called matrix protein. Two matrix proteins play a role in the assembly of the virus when it replicates: M1 protein, which belongs to the virus structure, and M2 protein, which has been detected in the complete virus but a considerable proportion of which is not integrated into the mature virus. In the present patent application, the expression "M protein" designates the matrix protein found major in the complex virus, that is to say M1 protein, which may or may not be mixed with other proteins or core fractions. SUMM M protein, which may constitute the additive to the vaccine according to the invention, may be prepared according to known techniques of protein separation and purification; for example, a

method.

SUMM

treating a core suspension with a surfactant, for example a

nonionic surfactant, at a sufficiently high concentration and

at a sufficiently acid pH to favour separation of proteins M and NP in.

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concentrating the supernatant if desired, in order to obtain a core
       fraction solution constituting an additive for a vaccine
       composition according to the invention.
SUMM
       The nonionic surfactant used is for example a
       polyoxyethylenated alkyl-phenol- such as Triton X 100 (Rohm & Haas), a
       polyoxyethylenated fatty alcohol such.
SUMM
             . in order for the additive to be present in effective amount in
       a volume compatible with its administration as a vaccine. If
       necessary, the detergent may be eliminated, for example by
       dialysis.
      The resulting, possibly concentrated supernatant may be used as an additive, in sufficient quantity to obtain an improvement in the \dot{}
SUMM
       vaccination. The quantity of this additive may be assessed for
       example by reference to the quantity of M protein contained therein.
      The core fractions may also be lipid-free core fractions which may be
       obtained by gentle treatment of the virus by at least one
       surfactant, generally used at weak concentration, for example
       nonionic surfactants such as those commercialized under the
       name NONIDET P40 or TRITON X100, or certain cationic surfactants
       such as hexadecyl trimethyl ammonium bromide. Suitable concentrations
       may be determined in each case by routine experiments; they are
       concentrations.
       When the vaccine additive according to the invention is in the
SUMM
       form of core particles, these may be core particles obtained through
       The vaccine composition of the invention may be administered
SUMM
       to humans or animals likely to suffer from influenza, notably equine,
       swine and avian species. The doses of the composition to be administered
       are the usual ones for this type of vaccine, and may if
       necessary to determined for animals in each case by routine experiments.
SUMM
       For example, in humans, the unit doses for the first constituent
       (conventional vaccine) are generally defined by their content
       of hemagglutinin. For each of the three types of vaccine (
       vaccine with complete virion, sub-unit vaccine and
       split vaccine) they generally correspond to 1-20 .mu.g, and
       particularly 5-20 .mu.g, for example 10-15 .mu.g of hemagglutinin of
       each of the.
      The quantity of additive, in the vaccine composition of the
SUMM
       invention, is a predetermined quantity sufficient to cause a
       statistically significant improvement in the efficiency of the
       vaccination in the animal species concerned.
SUMM
      The quantity of additive to be used with a unit dose of vaccine
       is for example a quantity sufficient to cause a statistical improvement
       of at least 5%, particularly at least 10%, in vaccination
       efficiency, assessed over at least one recognised ctiterion of
       vaccination efficiency. The efficiency of the
       vaccination may be determined for example by epidemiological
       studies of a population vaccinated with a conventional
       vaccine, a population vaccinated with the conventional
       vaccine and the additive, and possibly a non-vaccinated
       population. The criteria chosen for assessment of vaccination
       efficiency are those commonly used by those specialized in this field
       and particularly:
SUMM
       the proportion of vaccinated individuals suffering from an
       influenza affection, compared to the total number of individuals
       vaccinated, in a region where an influenza epidemic has indeed
       develope;
SUMM
       or protection against a virus subtype other than the.
       subtype(s) used in the preparation of the components (conventional
       vaccine and additive) of the vaccine,
SUMM
       or else the improvement of the effectiveness of the vaccine
       may be evaluated through a statistically significant enhancement of the
       immune response, as assessed by the pourcentage of sero-converted
       subjects, by the amount of antibodies directed against the influenza
       virus or components thereof, or by tests measuring the
       immunocompetent cell response to the influenza virus
       infection.
SUMM
      With certain animals species, particularly laboratory animals or with
       volunteers, it is also possible to determine the efficiency of a
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vaccination by using experimental infection.

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SUMM
             . the said quantity of core particles, or else a quantity of the
       said fraction having the same activity in the vaccine
       composition as the said quantity of core particles).
SUMM
       When the additive is at least one M protein, or a core fraction
       containing M protein, the unit dose of vaccine composition
       preferably contains at least 3-5 .mu.g, and particularly at least 7-10
       .mu.g of added M protein (that is to say in addition to the free.M
       protein possibly already present in the conventional vaccine,
       notably when it is a split vaccine). The quantities of M
       protein indicated are assessed notably by an immunological test
       according to the ELISA technique. The amounts.
                                                       . . quantified, e.g.
       with bicinchonic acid. One may also proceed by comparison with the M
       protein content of a purified influenza virus, subjected to a
       detergent treatment, by assuming that the M protein represents
       50% by weight of the total proteins in the virus. The ELISA
       tests are carried out on tested preparations or on control preparations
       of M protein of virus, in a solution containing for example
       0.1% sodium dodecyl sulfate (SDS). The total proteins are dosed for
       example by any.
SUMM
      It is known that vaccines with complete virions, and sub-unit
       vaccines are virtually free from free M protein (that is to say,
       outside the core or virus particles). Conventional split
       vaccines contain certain quantities of M protein, these
       quantities being variable and depending mainly on the preparation
       technique used.
       Thus, it is easy to determine the quantities of M protein which have
SUMM
       been added to a given vaccine composition, by knowledge of the
       preparation technique used, and thus of the quantities of free M protein
       normally present in the vaccine composition obtained by the
       said technique.
SUMM
             . measured e.g. in saccharose gradient) which is generally
       different from that of the M protein already present in the split
       vaccine composition.
       It may be administered in association with other vaccines
       and/or additives.
SUMM
       The composition may also be used for booster injections, for example 1
       to 3 months after the first vaccination.
SUMM
       Another object of the invention is the use of an additive constituted by
       core of at least one influenza virus or by a fraction of core
       of at least one influenza virus, in the preparation of a
       vaccine composition against influenza comprising a conventional
       influenza vaccine.
SUMM
             . particularly concerns use of a second constituent (additive)
       containing core, or a purified core fraction, of at least one influenza
       virus, in the preparation of a vaccine composition
       against influenza containing a first constituent corresponding to a
       conventional influenza vaccine, it being possible for the said
       first and second constituents to be present in one and the same
       container, or.
DRWD
       FIG. 2 shows a comparison of influenza vaccine profiles (one
       dose) before (a) and after (b) addition of 10 .mu.g viral core
       (FIG. 2 is comprised of six graphs: graph la, FIG. 2.1a shows
       vaccine profile before addition of vaccine core, with
       vaccine being complete virions; graph 1b, FIG. 2.1b shows
       vaccine profile after addition of vaccine core, with
       vaccine being complete virions; graphs 2a and 3a, FIGS. 2.2a and
       2.3a sow vaccine profile before addition of vaccine
       core, with vaccines being split vaccines; and graphs
       2b and 2b, FIGS. 2.2b and 2.3b show vaccine profile after
       addition of vaccine core, with the vaccines being
       split vaccines).
DETD
       Obtaining Purified Viral Core
DETD
       The reassortant strain of influenza virus NIB16 (A/H1N1) was
       used: said strain originates from mating wild strains A/Taiwan/1/86
       (A/H1N1) and reassortant X31 (A/H3N2), the latter being obtained by
       mating strain A/Alchi/2/68 with the A/Porto-Rico/8/34 (A/H1N1)
       virus.
DETD
       The viral suspensions were prepared by multiplication on chick
       embryonated eggs, concentration by ultrafiltration and purification on
       saccharose gradient as described in. .
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To extract the core, the purified virus, suspended in phosphate buffer pH 7.4 (PBS buffer), is subjected to two or three successive treatments with bromelain (Sigma) at. . . in 0.1M tris
DETD
       buffer pH 7.5, 1 mM EDTA, 50 mM beta-mercaptoethanol. For the first
       treatment with the protease, the viral suspension, adjusted to
       contain 2 mg of proteins per ml of buffer solution, is used, and 1 mg/ml of bromelain is added. After 2 hours' incubation at 37.degree. C. and
       dilution with an aqueous solution of 0.1M NaCl, the
       preparation is subjected to separation by ultra-centrifugation at
       120,000 g, for 90 min, at +4.degree. C..
                 20-60% (w/w) linear saccharose gradient in PBS buffer at
DETD
       100,000 g, for 16 hours, at +4.degree. C. The fractions containing
       viral core are diluted by one third with PBS buffer, then
       subjected to ultra-centrifugation at 120,000 g for 90 minutes, at.
DETD
       hemagglutinating activity is less than 0.01% that of the original
       virus (measurement by hemagglutination according to the method
       described by Palmer et al., Advanced Laboratory Technicals for Immunological Diagnostic, U.S. Dept. . .
DETD
       the final vaccine is prepared by diluting in PBS buffer, as
       indicated in example 2 below.
DETD
       Preparation of the Vaccine and Pharmacological Study
DETD
       As first constituent of the vaccine composition an inactivated
       monovalent split vaccine, obtained with the NIB16 strain, was
       used.
DETD
       This split vaccine was obtained by treating the virus
       with the mixture of Polysorbate 80 and ether, according to the method
       described in French patent 2 201 079 (example.
DETD
       The monovalent vaccine and the core were diluted and mixed in
       PBS buffer to provide the combinations and doses indicated in tables 1.
DETD
       The doses of split vaccine and core used are expressed in
        .mu.g of total proteins determined by colorimetry, by comparison with a
       standard solution of.
DETD
       One month after vaccination, the mice were infected with the
       A/Wilson Smith/33 (A/HlN1) strain, obtained from the World Influenza
       Centre in London. This strain.
                 groups were recorded in tables 1 and 2. In the experiments in
DETD
       table 1, no control mouse (unvaccinated) survived. The viral
       core administered alone had at best a limited protective effect
       (10-20%), and the split vaccine injected alone only protected
       30 to 50% of the mice. It may be seen that several of the split and core
       vaccine combinations gave synergic protection at concentrations
       higher than 3 .mu.g of split vaccine associated with 90 .mu.g
       of core, or else, 10 .mu.g of split vaccine associated with 10
        .mu.g of core.
       The increased survival obtained by associating split vaccine and core is statically significant. The results were subjected to
DETD
       variance analysis (FISCHER-SNEDECOR test F), which showed that the
       addition of core has a statistically significant synergic effect
       (p=0.027) on survival of the vaccinated mice.
       The experiment was repeated, reducing the range of core quantities
       tested in associated with the split vaccine. The results are
       presented in table 2. From the results in table 2, it may be seen that
       the addition of 3 .mu.g of core or more to the vaccine
       systematically increases the percentage of mice surviving the test
       (highly significant protection synergy: p test F=0.009). TABLE 1
DETD
Surviving mice/Tested mice
after immunisation, with, per mouse:
             with added core (.mu.g):
Split
  Vaccine (.mu.g)
             0
                     10
                                 30
                                        90
0 (only PBS)
             0/10
                     1/10
                                 2/10
                                        2/10
                                 3/10 8/10
 3
             3/10
                     2/10
                                 10/10.
10
             4/10
                     7/9
DETD
                       TABLE 2
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Surviving mice/Tested mice after immunisation, with, per mouse: Split with added core (.mu.g): Vaccine (.mu.g) 0 10 0 (only PBS) 0/10 0/10 1/10 8/10 10/10 2/10 10 6/10 10/10 10/10

Detection and Quantification of the Influenza Virus Core The influenza vaccines of the invention are likely to contain lipid-free or complete influenza core particles and complete virions or protein sub-units in. DETD . gradient. In the present case, 14 ml tubes with a 12 ml 20-60% gradient (w/w in PBS) were used. The vaccine dose placed in the tubes was 1 ml in volume. DETD . Edition, Ed. R. C. Weast, GRC Press Inc.) give the apparent density of the particles. Characteristically, the density of the viral core (obtained according to the procedure of example 1) is 1.15-1.16 g/cm.sup.3 and that of the virus is 1.19-1.20 g/cm.sup.3, this corresponds to saccharose concentrations of 35-37% and 42-44% respectively. DETD In order to confirm that the peak observed for a saccharose concentration of 35-37% is viral core, polyacrylamide gel electrophoresis (Laemmli, see above) may be used, after denaturing treatment of the sample by SDS at 2%,. DETD In FIG. 2, the diagrams obtained with 3 different vaccines are shown: a vaccine with complete virions, commercialized under the trade name Vaccin Grippal Ronchese (VGR), and two split vaccines obtained with different techniques and commercialized under the trade names VAXIGRIP and MUTAGRIP, these diagrams being established according to the. . . same principles and in the same recording conditions as those described concerning FIG. 1. FIG. 2 allows comparison of influenza vaccine profiles (one dose) before (a) and after (b) addition of 10 .mu.g of viral core. In FIG. 2, graph 1 corresponds to the vaccine with complete virions, and graphs 2 and 3 to the split vaccines (Vaxigrip and Mutagrip respectively). The profiles vary from one vaccine to another but none of them have a content of core. Preparation of a Core Fraction Containing a Matrix Protein (M Protein); DETD Vaccination and Dosage Tests DETD This fraction is extracted form purified viral core according

to a technique adapted from Ruigrok and coll. (1989). The core is suspended in PBS buffer adjusted to. . acetate buffer) may be added, to avoid later degradation of the M protein. The core is then subjected to a detergent treatment by a 10% solution of lubrol (Brij 36T, Sigma) the final concentrations of core, lubrol and where necessary TLCK.

DETD Sparrman et al., (1988). It consisted in capturing the Mprotein in the samples to be dosed (for example: influenza virus vaccine, core, purified proteins) using specific anti-M immunoglobulins adsorbed on microtitration plates; the presence of the M protein was then assessed using a succession of stages which led to a colorimetrical reaction proportional to the quantity of antigen present.

DETD Total anti-influenza virus M protein immunoglobulins: these specific immunoglobulins were obtained form serum from rabbits hyperimmunized by 3 injections respectively of 100, 75. . . . mu.g of M protein prepared as previously described; these injections were made intra-muscularly at monthly intervals in presence of Freund's adjuvant (complete adjuvant for the first injection and incomplete for the subsequent ones). The total immunoglobulins were then precipitated with ammonium sulphate at.

DETD Groups of six-week-old BALB/c mice (from IFFA-Credo, France) were immunized with preparations of Vaxigrip (monovalent A/H1N1 NIB16), with viral protein M, or by associations of Vaxigrip and M protein (see doses used in the result tables). The various preparations were administered subcutaneously under 0.5 ml without adjuvant and

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in a single injection. The mice were tested 4 to 5 weeks after
        immunization with 5 50% lethal doses.
DETD .
       The two tables presented correspond to two series of experiments carried
       out with the same M and NIB16 virus core protein preparations.
       They show that the association of Vaxigrip (monovalent NIB16) and matrix
       protein preparation improves the protection.
       The doses of vaccine, core and protein are expressed in .mu.q
       of total proteins determined for the vaccine and the core by
       Bradford's technique (1976, op. cit. in patent), and for M protein by
       dosage with bicinchonic acid.
DETD
                       TABLE 3
No of surviving mice/No of tested mice
(10 unless otherwise stated)
               NIB16 M protein (.mu.g)
  Vaccine
NIB16 (.mu.g)
                                   15
\overline{\phantom{a}}
                            1/9
                                   7/9
10
             0
DETD
                       TABLE 4
No of surviving mice/10 tested mice
NIB16 vaccine
                     NB16 M protein
(.mu.g)
                     0
                            5 .mu.g
0
                            n
                     1
10
                            9
DETD
       The mice may also be immunized using vaccine preparations with
       complete virions. The table below presents survival of BALB/c mice
       immunized at age 6 weeks with trivalent VGR vaccine
       preparations with complete virions (Vaccin Grippal Ronchese
        from the 1990-91 season). The trivalent vaccine dose used was
       about 5 .mu.g hemagglutinine of NIB16 virus per mouse; it was
       quantified by radial immunodiffusion according to the technique of Wood
       & coll., op. cit., and corresponds. . . . show that the improvement effect in protection by addition of M
DETD
       protein preparation may also be observed with a complete virus
       vaccine:
DETD
                       TABLE 5
No of surviving mice/10 mice tested
Complete virion
VGR vaccine M Protein NIB16 (.mu.g)
(.mu.g HA NIB16)
              0
                             5
                                    15
ō
              0
                             0
                                    C
              2
       In the same way as before, the BALB/c mice were immunized using sub-unit
DETD
       vaccine preparations, such as the DUPHAR vaccine
        (Influvac sub-unit); this is obtained after treatment of the
       virus by hexadecyl trimethyl ammonium bromide (Jennings, Smith
       et al, 1984; Bachmayer, 1975) and purification of the HA and NA
        glycoproteins.
       This sub-unit vaccine may be associated with core particles or
DETD
        a core fraction containing M protein using equivalent doses to those in
       the previous tests, i.e. for the monovalent or trivalent vaccine: the equivalent of 5 .mu.g of HA of virus NIB16 assessed by radial immunodiffusion; for the M protein: 5, 15 or 30 .mu.g of protein
       dosed by the bicinchonic.
       Bachmayer, H. (1975). "Selective solubilization of hemagglutinin and
DETD
       neuraminidase from influenza viruses." Intervirology, 5,
       260-272.
       Bucher, D. J., Kharitonenkov, I. G., Wajeed-Khan, M., Palo, A., Holloway, D. and Mikhail, A. (1987). "Detection of influenza
DETD
       viruses through selective adsorption and detection of the M
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DETD

protein antigen." J. of Immunol. Methods, 96, 77-85.

Jennings, R., Smith, T. L., Spencer, R. C., Mellersh, A. M., Edey, D.,
Fenton, P., et al (1984). "Inactivated influenza virus vaccines in man: a comparative study of subunit and split vaccines using two methods for assessment of antibody

responses." Vaccine, 2, 75-080.
Ruigrok, R. W. H., Calder, L. J. and Wharton, S. T. A. (1989). "Electron DETD Microscopy of the Influenza Virus Submembranal Structure." Virology, 173, 311-316.

Improvement of Protection against a Sub Type of the Influenza DETD Virus by use of a Different Sub-Type vaccine Containing Core

DETD Groups of OF1 male mice aged 6 weeks were treated with preparations of monovalent Vaxigrip A/H3N2.times.97, A/H3N2.times.97 virus core, or with associations of Vaxigrip and core. The different preparations were administered subcutaneously under a volume of 0.5 ml, without adjuvants and in a single injection. The mice were tested 5 weeks after immunization with a dose corresponding to 20 50%.

DETD TABLE 6

No surviving mice/no tested mice (10 unless otherwise stated) core X97 added (.mu.g)

Vaccine X97 (.mu.g)

	· ·	J	10	30
0	0/9	0/9	0	0
8	0 .	0	0	0/9
10	1	3	3	1
2.0				

as expected, vaccine A/H3N2 X97 does not afford protection DETD against an infection challenge with virus A/H1N1. A surprising effect of protection synergy is observed however when the vaccine is associated with core.

CLM What is claimed is:

- 1. In a vaccine composition which comprises an anti-influenza vaccine selected from the group consisting of a complete virion vaccine, a sub-unit vaccine, and a split vaccine, wherein the improvement comprises having an additive selected from the group consisting of: M protein from at least one influenza virus strain; an isolated influenza virus core particle including M protein from at least one influenza virus strain; and an isolated portion, including M protein, of an influenza virus core particle, from at least one influenza virus strain.
- 2. A method for inducing an immunological response in a host comprising inoculating said host with the vaccine composition according to claim 1.
- 3. A vaccine composition according to claim 1, wherein said anti-influenza vaccine is a complete virion vaccine.
- 4. A vaccine composition according to claim 1, wherein said anti-influenza vaccine is a split vaccine.
- 5. A vaccine composition according to claim 1, wherein said anti-influenza vaccine is a sub-unit vaccine.
- 6. A vaccine composition according to claim 1 wherein it is presented in the form of a unit dose containing an immunologically effective amount of the additive sufficient to effect enhancement of the anti-influenza vaccine.
- 7. A vaccine composition according to claim 6 wherein it contains as the additive at least 3-5 .mu.g of M protein.
- 8. A vaccine composition according to claim 6 wherein it contains as the additive at least 7-.mu.g of M protein.

- 9. A vaccine composition according to claim 6 wherein its anti-influenza vaccine component contains from 1 to 20 .mu.g of hemagglutinin of each of the strains of which it is composed.
- 10. The ${\bf vaccine}$ composition of claim 1 wherein the additive comprises isolated M protein.
- 11. The vaccine composition of claim 1 wherein the additive comprises an isolated portion of an influenza virus core particle.
- 12. The vaccine composition of claim 1 wherein the additive comprises an isolated influenza virus core particle.
- 13. A method for inducing an immunological response in a host comprising inoculating the host with the **vaccine** composition of claim 10.
- 14. A method for inducing an immunological response in a host comprising inoculating the host with the **vaccine** composition of claim 11.
- 15. A method for inducing an immunological response in a host comprising inoculating the host with the **vaccine** composition of claim 12.
- 16. A vaccine composition according to claim 10, wherein said anti-influenza vaccine is a split vaccine.
- 17. A vaccine composition according to claim 10, wherein said anti-influenza vaccine is a sub-unit vaccine.
- 18. A vaccine composition according to claim 10, wherein said anti-influenza vaccine is a complete virion vaccine.
- 19. A vaccine composition according to claim 11, wherein said anti-influenza vaccine is a split vaccine.
- 20. A vaccine composition according to claim 11, wherein said anti-influenza vaccine is a sub-unit vaccine.
- 21. A vaccine composition according to claim 11, wherein said anti-influenza vaccine is a complete virion vaccine.
- 22. A vaccine composition according to claim 12, wherein said anti-influenza vaccine is a split vaccine.
- 23. A vaccine composition according to claim 12, wherein said anti-influenza vaccine is a sub-unit vaccine.
- 24. A vaccine composition according to claim 12, wherein said anti-influenza vaccine is a complete virion vaccine.
- 25. A vaccine according to claim 10, wherein it is presented in the form of a unit does containing an immunologically effective amount of the additive sufficient to effect enhancement of the anti-influenza vaccine.
- 26. A vaccine according to claim 11, wherein it is presented in the form of a unit does containing an immunologically effective amount of the additive sufficient to effect enhancement of the anti-influenza vaccine.
- 27. A vaccine according to claim 12, wherein it is presented in the form of a unit dose containing an immunologically effective amount of the additive sufficient to effect enhancement of the anti-influenza vaccine.
- 28. A vaccine composition according to claim 25 wherein it contains as the additive at least $3-5\ .mu.g$ of M protein.
- 29. A vaccine composition according to claim 26 wherein it contains as the additive at least 3-5 .mu.g of M protein.

- 30. A vaccine composition according to claim 27 wherein it contains as the additive at least 3-5 .mu.g of M protein.
- 31. A vaccine composition according to claim 25 wherein in contains as the additive at least 7-10 .mu.g of M protein.
- 32. A vaccine composition according to claim 26 wherein it contains as the additive at least $7-10\,$.mu.g of M protein.
- 33. A vaccine composition according to claim 27 wherein it contains as the additive at least 7-10 .mu.g of M protein.
- 34. A vaccine composition according to claim 25 wherein its anti-influenza vaccine component contains form 1 to 20 .mu.g of hemagglutinin of each of the strains of which it is composed.
- 35. A vaccine composition according to claim 26 wherein its anti-influenza vaccine component contains from 1 to 20 .mu.g of hemagglutinin of each of the strains of which it is composed.
- 36. A vaccine composition according to claim 27 wherein its anti-influenza vaccine component contains from 1 to 20 .mu.g of hemagglutinin of each of the strains of which it is composed.
- 37. An anti-influenza vaccine kit comprising as a first component at least one anti-influenza vaccine selected from the group consisting of a complete virion vaccine, a sub-unit vaccine, and a split vaccine, and, a second component selected from the group consisting of: M protein from at least one influenza virus strain; an isolated influenza virus core particle including M protein from at least one influenza virus strain; and an isolated portion, including M protein, of an influenza virus core particle, from at least one influenza virus strain.
- 38. The vaccine kit according to claim 37, wherein said first component and the second component are present in the same container.
- 39. The ${\bf vaccine}$ kit according to claim 37, wherein said first component and the second component are present in separate containers, placed in. . .
- 41. The kit of claim 37 wherein the second component comprises an isolated portion of an influenza virus core particle.
- 42. The kit of claim 37 wherein the second component comprises an isolated influenza virus core particle.
- 43. A vaccine kit according to claim 40, wherein said first component and the second component are present in the same container.
- 44. A ${\bf vaccine}$ kit according to claim 40, wherein said first component and the second component are present in separate containers, placed in. . .
- 45. A vaccine kit according to claim 41, wherein said first component and the second component are present in the same container.
- 46. A vaccine kit according to claim 41, wherein said first component and the second component are present in separate container, placed in. . .
- 47. A vaccine kit according to claim 42, wherein said first component and the second component are present in the same container.
- 48. A vaccine kit according to claim 42, wherein said first component and the second component are present in separate containers, placed in. . .
- 49. In a vaccine composition which comprises an anti-influenza vaccine selected from the group consisting of a complete virion vaccine, a sub-unit vaccine, and a split vaccine, wherein the improvement comprises having an additive

which includes M protein from at least one influenza virus strain wherein the additive is obtained by a process consisting essentially of: treating a core suspension with a surfactant, at a sufficiently high concentration and at a sufficiently acid pH to favor separation of proteins M and NP in. . . 50. The vaccine composition of claim 49 wherein the process for obtaining the additive further comprises concentrating the supernatant.

- 51. A method for inducing an immunological response in a host comprising inoculating said host with the **vaccine** composition according to claim 49.
- 52. A vaccine composition according to claim 49 wherein the surfactant is a nonionic surfactant.
- 53. A method for inducing an immunological response in a host comprising inoculating said host with the **vaccine** composition according to claim 50.
- 54. The vaccine of claim 52 wherein the nonionic surfactant is selected from the group consisting of polyoxyethylenated alkylphenols, polyxyethylenated fatty alcohols and alkyl-osides.
- 55. A method for inducing an immunological response in a host comprising inoculating said host with the **vaccine** composition according to claim 54.
- 56. A method for inducing an immunological response in a host comprising inoculating said host with the **vaccine** composition according to claim 52.

IT 9002-92-0

(in M protein sepn. for influenza vaccine component)

=> d bib abs hitstr 19

CN

ANSWER 19 OF 28 USPATFULL 97:38423 USPATFULL ΑN Detergent-facilitated immunoassay for the rapid and TΙ quantitative assay of pharmacological agents ΤN Cheng, Anthony K., Anaheim, CA, United States Kim, Julie S., Placentia, CA, United States Oh, Chan S., Chino Hills, CA, United States PA Beckman Instruments, Inc., Fullerton, CA, United States (U.S. corporation) 19970506 PΙ US 5627080 US 1994-283116 19940729 (8) ΑI DTUtility FS Granted Primary Examiner: Green, Lora M.; Assistant Examiner: Wolski, Susan C. **EXNAM** LREP May, William H., Hampson, Gary T. Number of Claims: 28 CLMN Exemplary Claim: 1 ECL 1 Drawing Figure(s); 1 Drawing Page(s) DRWN LN.CNT 1403 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Methods for modulating the rates and dose responses of immunoassays through the incorporation of one or more detergents into the immunoassay reaction are disclosed. The methods are particularly suitable for automated immunoassay formats, especially with formats that use analyte-biotin bidentate reagents. The methods may be used to facilitate the detection of any desired, preselected pharmacological agent. CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 9002-93-1, Triton X-100 (detergent-facilitated immunoassay of drugs) RN 9002-93-1 USPATFULL Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me} & \text{O-CH}_2\text{-CH}_2 \\ \text{Me} & \text{Me} \end{array}$$

=> d bib abs hitstr 20

ANSWER 20 OF 28 USPATFULL 97:5959 USPATFULL AN TΙ Contraceptive compositions Brode, George L., Bridgewater, NJ, United States ΙN Doncel, Gustavo F., Norfolk, VA, United States Gabelnick, Henry L., N. Bethesda, MD, United States Kreeger, Russell L., Flemington, NJ, United States
Salensky, George A., White House Station, NJ, United States
Medical College of Hampton Roads, Arlington, VA, United States (U.S. PA corporation) Biomaterials Corporation, Plainsboro, NJ, United States (U.S. corporation) US 5595980 PI. 19970121 US 1995-418884 19950407 (8) ΑI RLI Continuation of Ser. No. US 1993-129253, filed on 29 Sep 1993, now abandoned DTUtility Granted FS Primary Examiner: Wityshyn, Michael G.; Assistant Examiner: Prats, EXNAM Francisco C. LREP Banner & Witcoff Ltd. Number of Claims: 8 CLMN Exemplary Claim: 1 ECL DRWN No Drawings LN.CNT 859 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Improved contraceptive compositions are disclosed which comprise a spermicide or virucide, a polymeric delivery component and optionally a cosmetic ingredient. The improvement is directed to the use of certain hydrophobically modified polysaccharides as the polymeric delivery component. Quite advantageously, the hydrophobically modified polysaccharides of the present invention can alter sperm motility. Moreover, the hydrophobically modified polysaccharides can provide reduced irritation potential when used in combination with spermicides such as, for example, nonoxynol-9, which may reduce the potential for infection of sexually transmitted diseases such as HIV and herpes. CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 26027-38-3, Nonoxynol-9 (contraceptive compns.) 26027-38-3 · USPATFULL Poly(oxy-1,2-ethanediyl), .alpha.-(4-nonylphenyl)-.omega.-hydroxy- (9CI) CN

$$O-CH_2-CH_2$$
 OH

Me- $(CH_2)_8$

=> d kwic 20

L74 ANSWER 20 OF 28 USPATFULL

(CA INDEX NAME)

SUMM . . . such increased risks of vaginal irritation, there may be increased risks of contracting sexually transmitted diseases of bacterial, fungal or viral origin, such as, for example, HIV and herpes.

DETD . . . 500 centipoise. Unless otherwise indicated, as used herein the term "viscosity" refers to the viscosity of a 2.0 weight percent aqueous solution of the polymer measured at 25.degree.

C. with a Brookfield viscometer. Such viscosity measuring techniques are

known to those skilled. DETD . . are known to those skilled in the art and are often referred to in the art as diluents, solvents and adjuvants. Typically cosmetic ingredients include, for example; water, ethyl alcohol, isopropyl alcohol, glycerin, glycerol propylene glycol, sorbitol and other high molecular. . . 0.1 to 5% weight based on the weight of the contraceptive compositions, of other additives, such as, for example; stabilizers, surfactants, menthol, eucalyptus oil, other essential oils, fragrances, and the like. Polyoxyethylene 20osorbitan monolaurate is a preferred stablizer for use in. sodium hydroxide solution containing 20 wt % sodium hydroxide DETD was added. After stirring for 30 minutes, 64 g of an aqueous solution containing 40 wt % HS1 was added. The reactor mixture was heated to 55.degree. C. and held there for 2 hours. Then 8.7 grams of an aqueous solution containing 70 wt % CS1 was added. The mixture was held at 55.degree. C. for another hour. The reaction was. . . with 3 grams glacial acetic acid. The reaction slurry was filtered and washed 7 times with 400 grams of an aqueous solution containing 90 wt % acetone, once with 400 grams of an aqueous solution containing 94 wt % acetone, and once with 400 grams of a solution containing 0.5 milliliter of a 40 wt. DETD One hundred gram ${\bf aqueous}$ ${\bf solutions}$ containing 1.5 weight percent of the polymeric delivery component being tested were prepared. To each solution, 4.16 grams of N-9. A contraceptive gel was prepared by mixing 2.5 g of a 2.5 wt % aqueous solution of POL. 2 with 2.5 g of 3 wt % DETD solution of POL. 3 and 0.2 g of N-9. A. DETD A contraceptive lotion was prepared by combining 62.5 grams of an aqueous solution containing 10 wt. % CL, 104.2 grams of an aqueous solution containing 6 wt. % POL. 1, 25.0 grams of P-20 and 808.3 grams of water. The resulting lotion contained 0.625. 3001-63-6, Quab 426 9003-39-8, PVP 9004-62-0, Hydroxyeth 9004-64-2, Hydroxypropyl cellulose 9036-19-5, Octoxynol-9 TΤ 9004-62-0, Hydroxyethyl cellulose **26027-38-3**, Nonoxynol-9 50744-78-0, Quab 342 29756-57-8, Nonylphenyl glycidyl ether (contraceptive compns.)

=> d bib abs hitstr 21

L74 ANSWER 21 OF 28 USPATFULL

90:11136 USPATFULL

ΤI Process for preparing immunogenic complexes and pharmaceutical

composition containing these complexes

TN De Vries, Petra, Almere, Netherlands

van Wezel, deceased, Antonius L., late of Bilthoven, Netherlands by

Cornelia M. van Wezel-Berendse, administratrix

Beuvery, Eduard C., Vianen, Netherlands De Staat der Nederlanden Vertegenwoordigd door de Minister van Welzion, PA

Volksgezondheid en Cultuur, Leidschendam, Netherlands (non-U.S.

corporation)

ΡI us 4900549 19900213

ΑI US 1987-3070 19870114 (7) 19860114

PRAI NL 1986-66

DT Utility

FS Granted

EXNAM Primary Examiner: Moskowitz, Margaret; Assistant Examiner: Kushan, Jeff

Brumbaugh, Graves, Donohue & Raymond Number of Claims: 15 LREP

CLMN ECL Exemplary Claim: 1

DRWN 10 Drawing Figure(s); 5 Drawing Page(s)

LN.CNT 419

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention relates to a process for preparing immunogenic complexes AB in which an amphiphatic antigenic protein or peptide in dissolved or solubilized form is contacted with a solution containing a detergent, a sterol, and a glycoside comprising hydrophobic and hydrophilic regions, in at least the critical micelle forming concentration, the detergent is removed, and the immunogenic complex formed is purified. Optionally, the solution with which the antigenic protein or peptide is contacted also contains a phospholipid, preferably phosphatidylethanolamine. The preferred sterol is cholesterol, and preferred glycosides are saponins, espeically Quil Α.

The immunogenic complex is useful as a vaccine. Its immunogenic power is higher than that of corresponding micelles formed by aggregation of the antigens, and is also higher than that of the antigens incorporated in liposomes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 9002-93-1, Triton X-100

(immunogenic complex-contg. micelles for vaccines formation with)

RN 9002-93-1 USPATFULL

Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl].omega.-hydroxy- (9CI) (CA INDEX NAME) CN

$$Me_3C-CH_2-CH_2$$
 OH $Me_3C-CH_2-CH_2$ OH $Me_3C-CH_2-CH_2$

=> d bib abs hitstr 22 L74 ANSWER 22 OF 28 USPATFULL 88:13242 USPATFULL ΔN Aryl and heteroaryl ethers as agents for the treatment of hypersensitive TI ailments Chakraborty, Utpal R., Orangeburg, NY, United States Youssefyeh, Raymond D., Tarrytown, NY, United States IN USV Pharmaceutical Corporation, Fort Washington, PA, United States (U.S. PΑ corporation) PΙ US 4728668 19880301 US 1986-877570 19860623 (6) ΑI Division of Ser. No. US 1985-723781, filed on 16 Apr 1985, now patented, RLI Pat. No. US 4631287 DТ Utility FS Granted EXNAM Primary Examiner: Friedman, Stanley J. Number of Claims: 6 Exemplary Claim: 1 CLMN ECL DRWN No Drawings LN.CNT 551 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The present invention is concerned with the therapeutic composition AB comprising as an active ingredient a compound of the formula: (R.sub.1) (R.sub.2) Ar--Z--M--Ar.sub.1 (R.sub.3) (R.sub.4) Iand salts thereof; wherein Ar and Ar.sub.1 are independently phenyl, naphthyl or a nitrogen, oxygen, or sulfur heterocyclic ring; ${\tt Z}$ is an alkylene chain containing from 1 to 5 carbon atoms in the principal chain and up to a total of 10 carbon atoms; M is oxygen, sulfur, or NR.sub.5; R.sub.1, R.sub.2, R.sub.3 and R.sub.4 are each independently H, lower alkyl, lower alkoxy, hydroxy, halo, trihalomethyl, hydroxy lower alkyl, carboxy, formyl, aryl, aryloxy, benzyloxy, lower alkanoyl, carboxy lower alkoxy, nitro, amino, lower alkylamino, dilower alkylamino, cyano, lower alkanoyloxy, carbamoyl, lower alkoxy-alkoxy, carbo-lower alkoxy-alkoxy, or tetrahydropyranylmethyl; and R.sub.5 is hydrogen or lower alkyl. CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 109-86-4, 2-Methoxyethanol (reaction of, with (chloromethyl)quinoline) 109-86-4 USPATFULL RN Ethanol, 2-methoxy- (8CI, 9CI) (CA INDEX NAME) CN

но-сн₂-сн₂-о-сн₃

=> d bib abs hitstr 24

```
ANSWER 24 OF 28 USPATFULL
T.74
AN
                      87:7997 USPATFULL
ΤI
                      Plasminogen activator derivatives
                     Shimizu, Kimihiro, Yoshikawa, Japan
Nakahara, Tsuguji, Tokyo, Japan
IN
                      Kinoshita, Taketoshi, Koshigaya, Japan
                      Takatsuka, Jun, Kawasaki, Japan
                      Igarashi, Michiko, Musashino, Japan
PA
                      Nippon Chemiphar Company, Ltd., Tokyo, Japan (non-U.S. corporation)
                     US 4640835
US 1983-546590
PΤ
                                                                                              19870203
AΙ
                                                                                               19831028 (6)
DCD
                      20020122
                      Continuation-in-part of Ser. No. US 1982-437009, filed on 27 Oct 1982,
RLI
                      now patented, Pat. No. US 4495285
DT
                     Utility
FS
                      Granted
EXNAM
                     Primary Examiner: Shapiro, Lionel M.
                     Oblon, Fisher Spivak, McClelland & Maier Number of Claims: 24
LREP
CLMN
ECL
                     Exemplary Claim: 1
DRWN
                     18 Drawing Figure(s); 13 Drawing Page(s)
LN.CNT 1329
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
                      Derivatives of a nonimmunogenic plasminogen activator which comprises at
AΒ
                      least one polyalkylene glycol group chemically bonded with at least one
                      coupling agent to amino acid side chains of said plasminogen activator,
                      wherein said polyalkylene glycol has a molecular weight of about
                      200-20,000 and is unsubstituted or is substituted with one or more
                     alkyl, alkoxy or alkanoyl groups or a mixture thereof.
                      The plasminogen activator derivatives have an extended circulating life
                      in the mammalian bloodstream and also inhibit the formation of thrombus
                      in the same.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 9004-74-4 9004-99-3 9005-00-9
                         (reaction of, with cyanuric acid chloride)
RN
                9004-74-4 USPATFULL
CN
               Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxy- (9CI) (CA INDEX
                     RN
                9004-99-3 USPATFULL
               {\tt Poly(oxy-1,2-ethanediyl),\ .alpha.-(1-oxooctadecyl)-.omega.-hydroxy-\ (9CI)}
CN
                      (CA INDEX NAME)
\label{eq:mechanical} \text{Me-} \text{(CH$_2$)}_{16} \\ \text{C} \\ \hline \\ \text{C} \\ \hline \\ \text{C} \\ \\ \text{O} \\ \text{CH$_2$} \\ \text{CH$_2$} \\ \hline \\ \text{CH$_2$} \\ \\ \text{OH} \\ \\ \text{OH} \\ \\ \text{OH} \\ \\ \text{OH} \\ \text{OH}
```



document some laury copds

CEPERLEY 09/647,518

=> d scan 113

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

IN 3,6,9,12-Tetraoxatetracosan-1-ol (6CI, 7CI, 8CI, 9CI)

MF C20 H42 O5

CI COM

 ${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me}$

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):22

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

IN Poly(oxy-1,2-ethanediyl), .alpha.-(2-octyltetradecyl)-.omega.-hydroxy(9CI)

MF (C2 H4 O)n C22 H46 O

CI PMS

$$\begin{array}{c|c} \text{CH}_2 & \hline & \text{O-CH}_2 - \text{CH}_2 \\ \hline & \text{Ne-(CH}_2)_{\, 7} - \text{CH-(CH}_2)_{\, 11} - \text{Me} \end{array}$$

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

IN 3,6,9,12,15,18,21,24-Octaoxahexatriacontan-1-ol (7CI, 8CI, 9CI)

MF C28 H58 O9

CI COM

HO-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O

PAGE 1-B

 $-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me$

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

IN Poly(oxy-1,2-ethanediy1), .alpha.-(4-dodecylpheny1)-.omega.-hydroxy- (9CI)

MF (C2 H4 O)n C18 H30 O

CI PMS, COM

Me- (CH₂)₁₁

$$0-CH2-CH2$$
o- OH

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

IN 3,6,9,12,15-Pentaoxaheptacosan-1-ol (6CI, 7CI, 8CI, 9CI)

MF C22 H46 O6

CI COM

PAGE 1-A

$${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-$$

PAGE 1-B

- (CH₂)₁₁-Me

23 ANSWERS REGISTRY COPYRIGHT 2001 ACS L13

Dodecanoic acid, 41-hydroxy-3,6,9,12,15,18,21,24,27,30,33,36,39-

tridecaoxahentetracont-1-yl ester (9CI)

C40 H80 O16

PAGE 1-A

PAGE 1-B

$$- \, \mathtt{CH_2} - \, \mathtt{CH_2} - \, \mathtt{O} - \, \mathtt{CH_2} - \, \mathtt{CH_2} - \, \mathtt{O} - \, \mathtt{CH_2} - \, \mathtt{CH_2} - \, \mathtt{O} - \, \mathtt{CH_2} - \, \mathtt{CH_2} - \, \mathtt{O} - \, \mathtt{CH_2} - \, \mathtt{CH_2} - \, \mathtt{O} - \, \mathtt{CH_2} - \, \mathtt{CH_2} - \, \mathtt{O} - \, \mathtt{CH_2} - \, \mathtt{CH_2} - \, \mathtt{O} - \, \mathtt{CH_2} - \, \mathtt{CH_2} - \, \mathtt{O} - \, \mathtt{CH_2} - \, \mathtt{CH_2} - \, \mathtt{CH_2} - \, \mathtt{O} - \, \mathtt{CH_2} - \, \mathtt{C$$

PAGE 1-C

REGISTRY COPYRIGHT 2001 ACS L13 23 ANSWERS

IN Dodecanoic acid, 17-hydroxy-3,6,9,12,15-pentaoxaheptadec-1-yl ester (9CI)

C24 H48 O8

PAGE 1-A

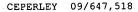
$${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-$$

PAGE 1-B

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS IN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT

(C2 H4 O)n C12 H26 O MF

PMS, COM CI



$$HO \longrightarrow CH_2 - CH_2 - O \longrightarrow n$$
 (CH₂)₁₁ - Me

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

IN Dodecanoic acid, 2-[2-(2-hydroxymethylethoxy)methylethoxy]methylethyl

ester (9CI) MF **C21 H42 O5**

CI IDS

 $\begin{array}{c} \text{O} \\ \text{HO-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-C-(CH}_2)} \\ \text{10-Me} \end{array}$

3 (D1-Me)

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS IN Dodecanoic acid, 2-hydroxyethyl ester (9CI) MF C14 H28 O3

 $\begin{array}{c} \text{O} \\ \parallel \\ \text{HO-CH}_2\text{--CH}_2\text{--O-C--(CH}_2)_{10}\text{--Me} \end{array}$

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS
IN Dodecanoic acid, 29-hydroxy-3,6,9,12,15,18,21,24,27-nonaoxanonacos-1-ylester (9CI)

MF C32 H64 O12

CI COM

PAGE 1-A

 ${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH$

PAGE 1-B

— CH₂— CH₂— O— CH₂— CH₂— CH₂— O— CH₂— CH

PAGE 1-C

- (CH₂)₁₀- Me

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS IN 3,6,9,12,15,18-Hexaoxatriacontan-1-ol (6CI, 7CI, 8CI, 9CI)

MF C24 H50 O7

CI COM

PAGE 1-A

HO-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-O-CH2-O-CH2-O-

PAGE 1-B

 $-CH_2-CH_2-O-(CH_2)_{11}-Me$

REGISTRY COPYRIGHT 2001 ACS

Dodecanoic acid, 20-hydroxy-3,6,9,12,15,18-hexaoxaeicos-1-yl ester (9CI) IN

MF C26 H52 O9

PAGE 1-A

HO-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-O-CH2-CH2-O

PAGE 1-B

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

IN Ethanol, 2-[2-(dodecyloxy)ethoxy]- (6CI, 7CI, 8CI, 9CI)

C16 H34 O3 MF

CT COM

$${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me}$$

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

IN Poly(oxy-1,2-ethanediy1), .alpha.-(1-oxododecy1)-.omega.-hydroxy- (9CI) ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT

(C2 H4 O)n C12 H24 O2 MF

CI PMS, COM

Me-
$$\{CH_2\}_{10}$$
- C - CH_2 -

REGISTRY COPYRIGHT 2001 ACS L13 23 ANSWERS

IN Dodecanoic acid, 26-hydroxy-3,6,9,12,15,18,21,24-octaoxahexacos-1-yl ester

(9CI)

MF C30 H60 O11

PAGE 1-A

PAGE 1-B

$$- \text{CH}_2 - \text{CH}_2 - \text{O} - \text{C} - \text{(CH}_2)_{10} - \text{Me}$$

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

Ethanol, 2-(dodecyloxy)- (6CI, 7CI, 8CI, 9CI)

C14 H30 O2

 $HO-CH_2-CH_2-O-(CH_2)_{11}-Me$

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

Dodecanoic acid, 23-hydroxy-3,6,9,12,15,18,21-heptaoxatricos-1-yl ester (9CI)

C28 H56 O10

PAGE 1-A

PAGE 1-B

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

IN 3,6,9,12,15,18,21-Heptaoxatritriacontan-1-ol (6CI, 7CI, 8CI, 9CI)

MF C26 H54 O8

CT COM

PAGE 1-A

PAGE 1-B

$$-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me$$

L13

23 ANSWERS REGISTRY COPYRIGHT 2001 ACS
Dodecanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (9CI) IN

MF C18 H36 O5

$$\begin{array}{c} \text{O} \\ || \\ \text{HO-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-O-C-(CH}_2)_{10}\text{-Me} \end{array}$$

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

IN Ethanol, 2-[2-[2-(dodecyloxy)ethoxy]-(6CI, 7CI, 8CI, 9CI)

MF C18 H38 O4

CI COM

$${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{11}-Me}$$

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS

IN Dodecanoic acid, 2-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]ethyl ester (9CI)

MF C20 H40 O6

$$\begin{array}{c} \text{O} \\ \text{HO-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-CH}_2 \end{array}$$

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IN Dodecanoic acid, 2-(2-hydroxyethoxy)ethyl ester (9CI)

MF C16 H32 O4

CI COM

ALL ANSWERS HAVE BEEN SCANNED

d 5 can 2 5 some steanate CEPERLEY 09/647,518 Cpd5

=> d scan

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IN Octadecanoic acid, 2-hydroxyethyl ester (9CI)
MF C20 H40 O3
CI COM

O . || HO-CH2-CH2-O-C-(CH2)16-Me

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):18

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IN Ethanol, 2-[2-[2-(octadecyloxy)ethoxy]- (6CI, 7CI, 8CI, 9CI)
MF C24 H50 O4

 ${\rm HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{17}-Me}$

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IN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI)
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT
MF (C2 H4 O)n C18 H36 O2
CI PMS, COM

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IN Octadecanoic acid, 17-hydroxy-3,6,9,12,15-pentaoxaheptadec-1-yl ester (9CI)
MF C30 H60 O8
CI COM

PAGE 1-A

HO-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O

PAGE 1-B

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IN Octadecanoic acid, 41-hydroxy-3,6,9,12,15,18,21,24,27,30,33,36,39-tridecaoxahentetracont-1-yl ester (9CI)
MF C46 H92 O16

PAGE 1-A

$${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-$$

PAGE 1-B

PAGE 1-C

$$\begin{array}{c} \bullet \\ \parallel \\ -\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{C}-\text{(CH}_2)}_{16}-\text{Me} \end{array}$$

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IN Octadecanoic acid, 20-hydroxy-3,6,9,12,15,18-hexaoxaeicos-1-yl ester (9CI)

MF C32 H64 O9

CI COM

PAGE 1-A

PAGE 1-B

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IN Octadecanoic acid, hydroxy-, 2-hydroxyethyl ester (8CI, 9CI)

MF C20 H40 O4

CI IDS

$$^{\rm O}_{\parallel}$$
 HO-CH₂-CH₂-O-C-(CH₂)₁₆-Me

D1-- ОН

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IN Octadecanoic acid, 23-hydroxy-3,6,9,12,15,18,21-heptaoxatricos-1-yl ester

(9CI)

MF C34 H68 O10

PAGE 1-A

 ${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-C$

PAGE 1-B

 $-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{C}-\text{(CH}_2)}_{16}-\text{Me}$

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IN Octadecanoic acid, 2-[2-(2-hydroxymethylethoxy)methylethoxy]methylethyl

ester (9CI)
MF C27 H54 O5

CI IDS

3 (D1-Me)

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IN Octadecanoic acid, 2-(2-hydroxyethoxy)ethyl ester (9CI)

MF C22 H44 O4

CI COM

$$\begin{array}{c} \text{O} \\ \parallel \\ \text{HO-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-C--(CH}_2)_{16}\text{--Me} \end{array}$$

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IN Ethanol, 2-(octadecyloxy)- (6CI, 7CI, 8CI, 9CI)

MF C20 H42 O2

CI COM

$${\tt HO-CH_2-CH_2-O-(CH_2)_{17}-Me}$$

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IN Octadecanoic acid, 26-hydroxy-3,6,9,12,15,18,21,24-octaoxahexacos-1-yl

ester (9CI)

4F C36 H72 O11

PAGE 1-A

 ${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-C$

PAGE 1-B

L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS
IN Poly(oxy-1,2-ethanediyl), .alpha.-octadecyl-.omega.-hydroxy- (9CI)
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT
MF (C2 H4 O)n C18 H38 O

CI PMS, COM

$$HO \longrightarrow CH_2 - CH_2 - O \longrightarrow D$$
 (CH₂)₁₇ - Me

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IN Octadecanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (9CI)

MF C24 H48 O5

$$\begin{array}{c} \text{O} \\ || \\ \text{HO-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-CH}_2\text{--CH}_2\text{--O-C-(CH}_2)_{16}\text{--Me} \end{array}$$

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IN Ethanol, 2-[2-(octadecyloxy)ethoxy]- (6CI, 7CI, 8CI, 9CI)

MF C22 H46 O3

CI COM

$${\tt HO-CH_2-CH_2-O-CH_2-CH_2-O-(CH_2)_{17}-Me}$$

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IN Octadecanoic acid, 29-hydroxy-3,6,9,12,15,18,21,24,27-nonaoxanonacos-1-yl

ester (9CI)

MF C38 H76 O12

PAGE 1-C

— (СН₂)₁₆— Ме

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IN Octadecanoic acid, hydroxy-, monoester with 1,2-propanediol (8CI, 9CI)

MF C21 H42 O4

CI IDS

$$\begin{array}{c} \text{O} \\ || \\ \text{HO-CH}_2\text{-CH}_2\text{-O-C-(CH}_2)_{16}\text{-Me} \end{array}$$

D1-Me

р1− он

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N 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, mono[2-(octadecyloxy)ethyl]

ester (9CI)

MF C26 H48 O8

CI IDS

CM 1

$${\tt HO-CH_2-CH_2-O-(CH_2)_{17}-Me}$$

CM 2

$$\begin{array}{c} {\rm CO_2H} \\ | \\ {\rm HO_2C-CH_2-C-CH_2-CO_2H} \\ | \\ {\rm OH} \end{array}$$

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IN Octadecanoic acid, 2-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]ethyl ester
(9CI)

(9CI)

MF C26 H52 O6

$$\begin{array}{c} \mathsf{HO-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2$$

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=> d bib abs hitstr 8

- L48 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2001 ACS
- AN 1991:519977 HCAPLUS
- DN 115:119977
- ${\tt TI}$. Enhancing properties of surfactants on the release of carbamazepine from suppositories
- AU Fontan, J. E.; Arnaud, P.; Chaumeil, J. C.
- CS Dep. Pharmacotech., Fac. Sci. Pharm. Biol., Paris, 75270, Fr.
- SO Int. J. Pharm. (1991), 73(1), 17-21 CODEN: IJPHDE; ISSN: 0378-5173
- DT Journal
- LA English
- The effect of surfactants on physicochem. properties and on the release characteristics of carbamazepine from fatty suppositories was investigated in vitro. Four surfactants, polyoxyethylene 50-stearate (Simulsol M), polyoxyethylene 23-lauryl ether (Brij 35), and polysorbates 20 and 80, were examd. as adjuvants. The dissoln. rate was enhanced by all surfactants used. The dissoln. rate at 30 min increased from 54% without surfactant, to 100% with polysorbate 80 (2%). The liquefaction time could be the limiting factor for the dissoln. rate of carbamazepine. The better solubilizing effect of polysorbate 80 can be due to the better incorporation capacity of its micelle.